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Original Article

MORPHOLOGIC CHANGES IN CORONARY HEART DISEASE

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I. INTRODUCTION

THE incidence of coronary atherosclerosis varies amongst peoples inhabiting different regions of the world. What influence, race, climate, dietary habits, nature of work and occupation and effect of regional diseases have on the incidence of arteriosclerosis remains unsettled. That it is not restricted to declining years of life, and that young men are equally susceptible to the disease process is increasingly being recognized (French and Dock, 1944; Macdonald, 1941). The significance of heredity, defective lipid metabolism, and physiological stress are emphasized (Dock, 1946; Leary, 1935). Hypertension and diabetes mellitus certainly increase the incidence of the disease in the community. Clinical studies on coronary artery disease have been made since Herrick's (1912) original contribution on the subject, but the knowledge of its pathologic anatomy, owing to lack of standard technique, remained incomplete. It has been the experience of most pathologists that the routine methods of autopsy—dissection and serial sectioning of the coronary arteries—do not yield uniformly successful results. Injection of dyes and other substances into coronary arteries, followed by roentgenography and corrosion of the heart muscle, had equally important disadvantages. In the past few years refinements in pathologic technique and their application to the study of morphologic features of coronary artery disease have contributed greatly by elucidating the mechanism of angina pectoris, coronary failure, and myocardial infarction (Schlesinger, 1938, 1940, 1941; Blumgart *et al.*, 1940, 1941). The basic lesion in coronary artery disease is focal atherosclerosis which may narrow the arterial lumina at multiple points or occlude them slowly or suddenly by an atheromatous 'abscess', hemorrhage into the subintimal plaque followed by thrombosis or by a primary thrombosis. When the evolution of the pathologic process is gradual, inter-arterial anastomoses develop, and it is the recognition of this phenomenon which has altered the concept of coronary artery disease.

After having studied Schlesinger's technique (Schlesinger, 1938, 1941) of coronary artery injection, unrolling the heart, roentgenography and dissection, one cannot fail to be impressed by its eminent suitability for the study of the pathologic anatomy of coronary artery disease. In this paper, it is intended to review the literature on studies in coronary circulation on experimental and technical aspects, give an outline of the technique, briefly describe the observations and comment on them.

II. REVIEW OF THE LITERATURE ON EXPERIMENTAL AND TECHNICAL STUDIES IN CORONARY CIRCULATION

Towards the end of the nineteenth century, Cohnheim and von Schulthess-Rechberg (1881) reported their experiments on clamping of coronary arteries in curarized dogs. It was observed that such a procedure caused the heart to stop in diastole. During this period the experiments were designed to elucidate the manner of cardiac standstill. From their experimental studies of myomalacia cordis a few years later, they concluded that the coronary arteries were 'functional end arteries'. Baumgarten (1899) believed that the area of myocardial infarction corresponded to the anatomic distribution of the obstructed artery. This was, however, not confirmed by Hirsch and Spalteholz (1907) who ligated the anterior descending arteries of 8 dogs and 2 apes. The animals did not die following the operation, and it was found that the infarct was smaller than the area corresponding to the anatomic distribution of the occluded artery. They also demonstrated that the infarct healed in the experimental animals with restitution of cardiac function. Miller and Matthews (1909) reported the effect on the heart of experimental obstruction of the left coronary artery. Ligation of any one of the coronary arteries did not produce fatal results in his animals. The operation was done under ether anaesthesia. Karsner and Dwyer (1916) studied myocardial infarction and pointed to the irregular margin of the infarct as a probable indication of anastomosis. Smith (1918) concluded from experimental studies in dogs and interpretation of human material that there is collateral circulation between the coronary arteries. He commented on the survival of dogs even after tying a large branch of the coronary artery and discussed variability and small size of the lesion produced. Sutton and Davis (1931) made observations on experimental myocardial infarction. When the animal was rested for a week after ligation of a coronary artery, a firm scar was formed replacing the infarcted muscle. If the animals were exercised after the operation, there was thin scar tissue with bulging of the affected region of the myocardium. Mautz and Gregg (1937) studying the dynamics of coronary circulation following chronic occlusion of coronary arteries, observed that anastomotic channels developed

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to supply blood to the affected region of the myocardium. Mautz and Beck (1937) emphasized that when the artery was gradually occluded these collateral channels could enlarge sufficiently to prevent infarction completely.

Beck and Tichy (1935) produced adhesions between the heart and the parietal pericardium, omentum, and skeletal muscle. They concluded that when a collateral circulation was established through these adhesions, ligation of the right coronary artery produced infarction in a few instances only; and that the rest of the animals had no infarction at all. The degree of constriction applied to the artery affected the capacity of the collateral circulation. Blum *et al.* (1938) produced gradual occlusion of a coronary in experimental animals and found that in chronic occlusions of the anterior descending artery in the dog no infarction occurred in many animals.

The experimental studies on dogs by Blumgart, Gilligan and Schlesinger (1941) and Blumgart *et al.* (1942) on the effect of temporarily constricting the coronary artery showed the gross and microscopic features of myocardial infarction if the period of constriction lasted 25 to 45 minutes. The extent of ischaemic changes corresponded to the duration of occlusion. There is full experimental support for the finding that temporary loss of blood supply causes irreversible muscle changes and prolonged loss of blood supply causes muscle necrosis. Pigs' hearts correspond to the human in the absence of collateral channels under normal circumstances. Therefore these were used in these experiments.

Varying degrees of coronary artery constriction by ligature produced lesions identical with those human lesions caused by atherosclerotic narrowing and thrombotic occlusion. Some of the animals died after the operation. Sudden death of the animals in this procedure is possibly due to ventricular fibrillation, which may also explain sudden death in humans with coronary disease where the autopsy shows no infarction.

Animal experimentation has contributed materially to the knowledge of coronary artery disease. In the beginning the procedure of ligating the artery was frequently fatal.

Subsequently myocardial infarction was successfully produced and it was observed that the infarct was smaller than the region supplied by the vessel which had been occluded. Finally it was noted that when the occlusion occurs gradually over a period of time, there may be no myocardial infarction.

In 1921, Gross published a valuable monograph on 'the vascular supply of the heart in its anatomical and clinical aspects'. The coronaries were injected with barium sulphate solution in warm gelatine, the heart fixed in formalin, and roentgenogram taken of the injected vessels. Small branches and anastomoses were clearly visualized, even though there

was a great deal of vascular overlapping. From a study of the distribution of the vessels in different age groups he concluded that there was a regression of the right artery in old age. Further, in the heart of an average young person there are functioning anastomoses but they can not fully compensate for sudden cutting off of the blood supply to the myocardium. If the arterial obliteration is a slower process and the circulation good, the collateral channels dilate to preserve some, if not all, of the heart muscle. When the coronaries of an old person are obliterated, the patent anastomoses and arteries *telae adiposae* can often supply blood to the affected region. The most important aspect of this study was to stimulate further investigation which contributed much to clarifying clinical disease patterns pertaining to the coronary arteries.

In 1924, Spalteholz published his monograph 'Die Arterien der Herzward', wherein he described a completely different technique. This consisted of chrome yellow-gelatine injection into coronary arteries, fixation of the heart in formalin, bleaching in hydrogen-peroxide, and dehydration in alcohol. Then it was placed in benzene, cleared in a mixture of oil of winter-green and benzylbenzoate and finally all air and benzene removed in a special tank. By this procedure the myocardium was cleared and rendered semi-transparent and the opaque injected vessels could be easily traced. Unrolling the heart, so that it may be laid in one plane, was very helpful in following the arteries and their ramifications. His comment on Gross technique was that it did not adequately demonstrate the inter-coronary anastomoses.

Oberhelman and LeCount (1924) emphasized the variability of the distribution of the coronary arteries. They also observed that coronary sclerosis constituted the principal stimulus to the development of anastomoses, and that some hearts possessed a functioning collateral circulation. They pointed out that, in this respect, some hearts are better endowed than others to withstand sudden occlusion of coronary arteries. By perfusion and injection, Wearn (1940) and Wearn *et al.* (1933) demonstrated the existence of communications—arterio-luminals and arterio-sinusoids—between the coronary arteries and the heart chambers. However, the significance of this extensive capillary circulation of the heart is far from clear.

Grant and Viko (1929) injected gelatine and celloidin masses into thebesian openings on the inner aspect of the myocardium and demonstrated connecting channels between the heart chambers and the coronary arteries through the capillaries. Whitten (1928, 1930, 1930a) used celluloid and corrosion technique with differential coloring for the right and the left coronary arteries. He observed that in most hearts the right coronary artery also supplied blood to the posterior basal surface of the left ventricle, and

with occlusion of this branch or of the main stem itself, the infarct was located in the posterior wall of the left ventricle, not in the right ventricle. Furthermore, the right coronary artery is smaller and more superficial and its branches come off the main stem gradually; while the left artery is larger and has deep penetrating branches which come off at right angles to the main vessel. When a branch of the right artery supplied a part of the left ventricle, it lost its usual features and assumed those of the left coronary artery. 85 per cent of the hearts examined showed a constant anatomic pattern of coronary arteries, i.e. right coronary preponderant type. Saphir et al. (1935), from their very careful dissection studies of the coronary arteries on autopsy material and their correlation with clinical data, concluded that the most severe arterial lesions occurred in the anterior descending branch of the left coronary artery. When myocardial infarction was found, at least two branches of the artery supplying the area were involved. Infarcted areas in general were present in the region supplied by the vessel affected. Occasionally, a recent thrombus was discovered in one artery, while the infarct was located in an area supplied by another previously occluded artery—an example of, 'infarction at a distance'—obviously due to cutting off the blood supply in the collateral channels from the recently occluded artery. Infarction without occlusion occurred when the coronary artery was grossly narrowed and a great demand was put on the heart muscle by exercise, thus subjecting it to acute anoxia. Coronary sclerosis and myocardial fibrosis were constantly present in patients with angina pectoris. Further they emphasized that coronary thrombosis, myocardial infarction and coronary atherosclerotic obstruction are not anatomic equivalents of angina pectoris as these morphologic changes are also found in patients who never had angina.

In 1938, Schlesinger published his studies on coronary occlusions and anastomoses. He pointed out that the methods so far available were unsatisfactory. To solve the difficulty of portraying them adequately, he emphasized that 'it would be necessary to use a method capable of completely and simultaneously visualizing the entire coronary artery tree in a manner such that the whole course of each individual arterial branch could be studied for defects, narrowings, occlusions, and anastomoses'. This he made possible, after many experiments, by the use of a lead phosphate agar injection mass into the coronary arteries with pressure, temperature, and viscosity standardized.

Subsequently the heart is unrolled by a series of incisions so that it lies in one plane. During this procedure one can examine the valvular and endocardial morphologic alterations. Roentgenography of the injected coronary arteries in an unrolled heart eliminates the overlapping of

vessels and it is possible to follow each artery and its branches individually while examining for the presence of plaques, narrowings and occlusions. These are suggested by irregularities or defects in the outline of the vessels. Shadows cast by the calcified plaque vary, depending on the relative opacity of the injection mass and of the calcium in the plaque. Anastomotic channels may be suggested on the roentgenogram as fine lines extending from one artery to the other. These observations are checked by careful dissection which, however, is greatly facilitated by differentially tinted masses in the arteries, their ramifications and anastomotic channels. Non-dissectable anastomoses, however, can only be surmised by the presence of a coloured mass other than that which has been injected into the artery, or by the mixture of coloured masses. The regions of the heart containing the anastomotic vessels are invariably those in which arterial narrowing or occlusion has occurred. The collateral circulation is designed to compensate for the reduced vascular supply. Schlesinger and Zoll (1941) observed a significant difference between the observed incidence of coronary occlusions in the uninjected coronary arteries and in those studied by injection plus dissection technique. It was concluded that by the older methods of study, e.g. dissection, serial section, stereoscope roentgenography and arterial injection of coloured substances followed by clearing or corrosion, many important details are not shown.

III. TECHNIQUE

The injection mass consists of agar-agar base in which lead phosphate is incorporated for its radiopaque properties. The mass is tinted with methylene blue for injection into the left coronary artery and with basic fuchsin for the right coronary; so that the two arteries are outlined in distinctive colours. The mass remains fluid at 44°C. and penetrates uniformly through the pre-capillary arterioles. Injection of arteries is completed in 5 to 7 minutes. Immersion of the heart in an iced saline bath congeals the mass in the vessels so that during unrolling of the heart and dissection it does not run out.

(a) Preparation of stock solutions for making radiopaque lead phosphate agar mass.

1. Solution A.

Lead acetate [$\text{Pb}(\text{C}_2\text{H}_3\text{O}_2)_2 \cdot 3\text{H}_2\text{O}$], C.P.	.. 240 gm.
Distilled water	.. 688 cc.

Heat to dissolve, filter through paper, and allow to cool.

2. Solution B.

Disodium phosphate (Na_2HPO_4 anhydrous) C.P.	.. 96 gm.
Distilled water	.. 760 cc.

Heat to dissolve, filter through paper, and allow to cool.

3. Agar-agar solution.

Agar-agar (Difco)	.. 15 gm.
Distilled water	.. 100 cc.

Dissolve the agar-agar in the water in a large flask over a full flame, at first there is much frothing but as the agar dissolves frothing diminishes and ceases when solution is complete.

4. Phenolsulphthalein solution.

P.S.P.	.. 1 cc.
Alcohol 95 per cent	.. 9 cc.

Mix in a well-stoppered bottle.

For preparing the final mass take 200 cc. of solution A in a flask and mix well with 2 cc. of P.S.P. solution. Heat 140 cc. of solution B to dissolve the crystals and allow it to cool. Now mix solution B with solution A thoroughly to form a white creamy precipitate. Add from a pipette enough 10 per cent caustic soda solution to tint the precipitate a permanent pink. About 50 cc. should be required. Filter through a sieve (44 micra) washing with distilled water into a graduated flask. Whatever precipitate does not pass through the filter should be discarded. Allow the mass to settle to the 300 cc. mark and remove the supernatant fluid by suction. Now add 100 cc. of agar which has been liquefied by heat, mix well, and filter through a couple of layers of gauze into medicine bottles and store. Methylene blue and basic fuchsin should be added to the mass before starting injection.

(b) Cannulation and injection.

Both coronaries are cannulated carefully and the cannulae fastened securely. Warm the heart in a 44°C. saline bath. Wash the coronaries with warm saline at a pressure of 150 mm. Hg. Now inject both the coronaries simultaneously with warm mass at 150 mm. Hg. pressure. The injection is continued until the manometric reading remains constant for a few minutes at 150 mm. Hg. This takes about 5 to 7 minutes. To insure flow into the anastomoses, pressure in the left artery is reduced to zero and in the right maintained at the initial level. After a few minutes the pressures are reversed, i.e. low pressure in the right and high in the left. The cannulae are now clamped and disconnected maintaining pressure at 150 mm. Hg. Lift the heart out of the bath and place in iced saline for half an hour to congeal the mass in the vessels.

(c) Unrolling of heart.

The first incision passes along a line just to the right of the anterior inter-ventricular sulcus, starting at the pulmonary valve and ending at the apex. The next incision starts in the aorta between the right and left anterior cusps of the aortic valve, extending down about 1 cm. into the base of the septum. Now separate the septum from the ventricles anteriorly and posteriorly. Bisect the anterior leaflet of the mitral valve and continue the incision through

the mitral ring and aortic ring to separate the left aortic cusp from the posterior aortic cusp. The left auricle having been entered from below, the incision is carried parallel to the left side of the inter-auricular septum through the pulmonary veins, to unroll completely the left side of the heart. Divide the tricuspid ring between the anterior and medial leaflets, continue across the aortic ring to separate the anterior aortic from below, this incision is carried parallel to the side of inter-auricular septum through the superior vena to unroll the heart completely.

(d) Make roentgenogram of the coronary arteries by placing the heart with pericardial surface in contact with x-ray film. Technical factors: Tube—XP-I, fine focus, distance 42 inches, milliamps 20, K.V. 48. Medium cone, time one second, plain folder.

(e) Dissection. With a fine pair of scissors, open the arteries carefully making note of narrowings, calcification, occlusions and anastomoses. As the left coronary is filled with blue mass and right with red, it is easy to follow them, their ramification and anastomoses.

(f) Material for histological examination is collected from different parts of the myocardium and septum to study ischaemic changes caused by arterial obliterative processes.

IV. OBSERVATION

Material for study was provided by 14 cases which came to autopsy at the Beth Israel Hospital. The heart and its vascular supply were examined in great detail in each instance. Coronary arteries were injected with differentially tinted lead phosphate agar mass to visualize the left and right artery and any anastomoses distinctly. Subsequently the heart was unrolled to bring the vessels into one plane, a roentgenogram was taken, and the vessels were carefully dissected. The roentgenogram was particularly helpful in dissection. Three cases were omitted from analysis because of insufficient data. The remaining 11 cases are shown in table I. These have been placed in 3 groups according to the degree of arteriosclerosis present in the coronary arteries. In group A there are 3 hearts with slight coronary arteriosclerosis but no narrowings or occlusions; one of these has a myocardial infarction without arterial occlusion. Group B consists of 5 hearts with moderate coronary sclerosis and narrowing of the lumen but no occlusion. In two of this group there are evidences of anastomoses and one shows myocardial infarction without arterial occlusion. Group C hearts show marked coronary sclerosis. Two of the three have arterial occlusions and anastomoses, and one has 'infarction at a distance'. One case from each of the above groups has been selected to illustrate the morphologic alterations in the coronary arteries and the resulting disease patterns.

TABLE I

Number	Autopsy	Age	Sex	Group	Coronary sclerosis	Occlusion	Anastomosis	Infarct
<i>Group A</i>								
1	A48-36	61	M.	I	Slight	—	—	—
2	A48-37	36	M.	III	"	—	—	+
3	A48-35	80	M.	I	"	—	—	—
<i>Group B</i>								
4	A48-34	46	M.	I	Moderate	—	—	—
5	A48-29	62	F.	I	"	—	R-L*	—
6	A48-26	49	M.	I	"	—	—	—
7	A48-27	74	M.	I	"	—	R-L, L-R	+
8	A48-25	58	M.	I	"	—	—	—
<i>Group C</i>								
9	A48-30	70	F.	I	Marked	—	R-L	—
10	A48-24	61	F.	I	"	L.D.	L-L, L-R	—
11	A48-32	71	F.	I	"	L.D., R.C.	—	+

* Abbreviations are explained in the text.

ILLUSTRATIVE CASES

Case 2: Rheumatic heart disease, shortness of breath and jaundice

Clinical history.—A 36-year-old single male was admitted to the hospital for shortness of breath and jaundice. He was known to have rheumatic heart disease since the age of 5 with exertional dyspnoea of 14 years' duration and congestive failure of 3 years' duration. He had angina pectoris of 2 years' duration. Two days before entry into the hospital he had a sudden onset of jaundice with dark-coloured urine and clay-coloured stools. There was no pain but he experienced chilly sensations. Physical examination revealed a thin dyspnoic, orthopnoic, deeply icteric male. Temperature 100, pulse 80, with grossly irregular rhythm. Respiration 34. B.P. 130/70. The peripheral veins were distended. Examination of the chest revealed dullness over the right base and moist râles over both lung fields. The heart was enlarged to the anterior axillary line and the apex beat was located in the 6th left interspace. An apical systolic and an early diastolic low-pitched murmur were heard. The pulmonary second sound was split and accentuated. The liver was enlarged and tender. Ankle oedema was present. There was slight cyanosis of the finger nails.

Laboratory data.—Urine contained albumin, bile and granular casts. W.B.C. 6,500 c.mm. on admission, two days later 21,500 with 79 per cent polymorphs and eight days later 35,000 with 92 per cent polymorphs. Bilirubin 42.5, prothrombin time 26, thymol turbidity 24.5, cephalin flocculation positive, N.P.N. 66, plasma protein 6.7 (albumin 3.91, globulin 2.75), agglutination for Weil's disease negative. A roentgenogram of the chest showed marked enlargement of the heart, a prominent pulmonary artery, a considerable amount of fluid in the right pleural space and 'some suggestion of

infarction in the right lung'. His electrocardiogram showed 'auricular fibrillation, right ventricular hypertrophy and left ventricular hypertrophy'.

Pathology.—(Heart and coronary arteries, see figures 1 and 2, plate I). Heart weighs 705 gm. There is diffuse yellow coloration of the greatly enlarged and dilated heart. Dilatation of right ventricle and both auricles is particularly marked. Left ventricular cavity appears small and its wall hypertrophied. Ascending aorta is $\frac{1}{2}$ the diameter of the pulmonary trunk. There appears to be a diffuse fibrosis of the right ventricular myocardium. In the left atrium there are two ante-mortem well-organized adherent thrombi. Atheromatous patches are present in the ascending aorta and pulmonary artery, more marked in the latter. Mitral cusps are calcified and deformed. Chordæ tendineæ are shortened and thickened. Coronary arteries are normal essentially.

Comments.—This heart belongs to group 3, according to the basic pattern of the coronary arteries, which are essentially normal in this case except for the injection of the conus vessel by anastomosis from the left coronary artery. Roentgenogram shows the calcified mitral valve and the enlarged right heart. Anatomic basis for angina pectoris lies in inadequate coronary circulation to the enlarged right heart which is diffusely fibrosed. Anastomotic injection of conus vessel is significant in this connection.

Case 8: Bronchogenic carcinoma, hypertensive and arteriosclerotic heart disease

Clinical history.—A 58-year-old male entered the hospital with the chief complaint of 'cough and cold' of 3 weeks' duration. He had chronic cough for 3 years productive of small amounts of sputum. Two months ago sputum increased in amount, had hæmoptysis, anorexia, weakness, fatigue and dyspnoea. Three weeks ago he

noticed hoarseness without dysphagia. Past history revealed that he had an episode of severe precordial pain for which he was placed in bed rest for 6 weeks. Subsequently he experienced dyspnoea and angina radiating to left shoulder and slight orthopnoea. Seven months prior to entry he had tarry stools for which he was hospitalized, transfused and told that he had an ulcer. Physical examination showed an elderly man, dyspnoeic, orthopnoeic, and hoarse with obvious signs of recent weight loss. Fundic vessels were narrowed and tortuous and showed A-V nicking. Trachea was deviated to left. Chest was emphysematous and left side of chest lagged on respiration. There was dullness on percussion from the top of scapula downward and all over the left chest anteriorly including obliteration of Kernig's isthmus. B.P. 190/120. Pulse equal and regular at 104. No peripheral venous congestion. Soft moderately high pitched blowing systolic murmur heard in the 2nd right interspace transmitted into neck. A2 greater than P2. Clubbing of fingers present.

Laboratory data.—Urine contained albumin and traces of sugar. Fasting blood sugar 115 and two hours after meal 224 mg. 100 cc. Thoracentesis yielded 400 cc. orange coloured fluid of specific gravity 1020 and protein content 5.4 per cent. Roentgenogram of the chest showed findings consistent with malignancy originating from the upper lobe of the left lung and extensive lymphoglandular metastasis in the mediastinum involving left phrenic nerve and the pleura. Electrocardiogram showed posterior myocardial infarction.

Pathology.—(Heart and coronary arteries, see figures 3 and 4, plate II).

Both the ventricles are hypertrophied and dilated. Right auricle is also dilated. Atheromatous patches are present in the ascending aorta. Aorta, pulmonary, tricuspid, and mitral valves are essentially normal. Area of heart in which the pulmonic veins open is greatly thickened and appears to be involved in the tumour process but the lumina of the veins are patent. There is an area of white dense tissue involving the myocardium seen from the endocardial surface of the left ventricle posteriorly toward the base and at the apex posteriorly and anteriorly so as to involve the septum which is thinned at the apex. Tissue in this place cuts with resistance. Papillary muscles of left ventricle appear hypertrophied. At the beginning of the left descending artery there is a moderate narrowing of the lumen. There are diffusely scattered atheromatous plaques in all the three main coronary stems. The right coronary artery wall is calcified for about a distance of 4 cm. from its ostium. One large branch of the left circumflex artery is markedly narrowed and some distance beyond this there is partially organized adherent thrombus which is not occluding. Vessels distal to this are injected purple with red tips, denoting

right to left anastomosis which is non-dissectable. However there is dissectable anastomosis present between the cut branch of left descending and the conus vessel.

Comments.—The heart belongs to group II and weighs 421 gm. Conus vessel has separate mouth and is proximally injected purple and distally blue. The presence of healed infarct at the apex explains the severe precordial pain for which the patient was put at rest for 6 weeks. However no occlusion was detected in the left descending coronary to account for the infarct. Narrowing of this vessel in its beginning and diffusely scattered atheromatous plaques combined with exertion may explain the occurrence of infarction without occlusion. Heart muscle requirements for oxygen depend on the demands put on it. If this is greatly increased by exercise, emotion, food, cold and infection, vascular supply cannot be correspondingly increased owing to coronary arteriosclerosis or inadequate anastomosis; myocardial infarction results even though the vessels are patent. Also anaemia by diminishing the oxygen carrying capacity of blood and shock, haemorrhage and post-operative states by reducing the pressure in the coronary arteries may precipitate infarction in a heart with minimal coronary artery disease.

Another interesting feature in this heart is the presence of marked narrowing and organizing thrombus in one of the large branches of the left circumflex without infarction. This is due to adequate anastomotic circulation from the right coronary artery as seen by the presence of purple mass. Death of the patient is due to bronchogenic carcinoma metastasizing extensively in mediastinal lymph nodes, there being no evidence of coronary failure. In this case there are examples of myocardial infarction without coronary occlusion, coronary occlusion without infarction, and angina pectoris following infarction due to inadequate coronary circulation.

Case 11: Acute myocardial infarction, arteriosclerotic heart disease, angina pectoris, and diabetes mellitus

Clinical history.—A 71-year-old widow was admitted to the hospital because of chest pain of 24 hours' duration. She had hypertension but lately blood pressure had been within normal limits. Acute illness began 24 hours before admission with sudden onset of anterior chest, back and left shoulder pain, collapse, sweating and difficulty in breathing. Patient was known to have angina pectoris, diabetes, diaphragmatic hernia and peptic ulcer in her first hospital admission 8 years ago. Physical examination showed poor colour, cyanosis, rapid breathing, absence of pulse at the wrist and blood pressure could not be measured. Heart was enlarged on percussion but the sounds were inaudible. Liver was enlarged 2 fingers below the right costal margin.

The electrocardiogram in lead 2 showed tiny Q, wide notched QRS complex, elevated ST segment, late T wave inversion, P-R interval 0.2 seconds and arrhythmia due to premature beats. Clinical course was stormy and the patient expired 1 hour after admission.

Pathology.—(Heart and coronary arteries, see figures 5 and 6, plate III). The heart weighs 457 gm. Coronary arteries are markedly sclerotic. Right ventricle is dilated and left ventricular wall appears to be thickened. Ascending aorta shows atheromatous patches. All valve cusps are essentially normal. On the endocardial surface of the left ventricle posteriorly and adjacent to the septum is a necrotic and friable area containing haemorrhagic extravasation indicative of a recent myocardial infarction. In this area the septum is thinned and bulges into the right ventricular cavity. Papillary muscles in the left ventricle are hypertrophied. On the epicardial surface, there is no evidence of pericarditis, recent or old, nor increase in the amount of fat. On cutting into the posterior myocardium there is a 4 cm. by 2 cm. haemorrhagic and softened area over the mid-septum. The left descending artery shows complete old occlusion a little below the main stem—all branches distal to this point are filled with blue mass by retrograde injection, i.e. left to left anastomosis. Main stem distal to occlusion is slightly narrowed along its entire length and contains scattered atheromatous plaques. The left circumflex artery is essentially normal except for one or two points of narrowings. The right coronary artery is completely occluded at its ostium and extending for a distance of approximately 4 cm. by a fresh, non-adherent, partially organized and occluding thrombus with calcification of its wall. Just distal to occlusion the artery is narrowed by a calcified plaque and a short distance further there is an atheromatous abscess. The remaining main stem contains scattered plaques and one point of slight narrowing. The greater part of main stem and branches are uninjected; however, the most distal part of main stem and its most posterior ventricular branch are filled with blue mass by retrograde injection, i.e. left to right anastomosis. Branches of right coronary artery are essentially normal except for one branch which is completely occluded and calcified at its origin.

Comments.—This heart provides an excellent illustration of 'infarction at a distance'. The left descending artery is completely occluded by an old thrombus and yet there is no evidence of infarction in the area of myocardium supplied by this vessel. This is due to the anastomotic channels from the left circumflex as shown by blue mass incompletely filling the vessel distal to the site of obstruction brought about by gradually evolving atherosclerotic occlusion. Necessary nutrition was supplied to the gravely endangered myocardium by the development of

above adaptive mechanism. The left ventricular myocardium posteriorly, however which in this group I heart is supplied by the right coronary artery, became the site of fatal infarct on this vessel becoming occluded by a fresh thrombus. There was not enough collateral circulation in this area to prevent infarction. It should be noted that the posterior part of the right ventricular myocardium also supplied by the occluded right coronary is not affected. Diabetes mellitus and hypertension of many years' duration are evidently the sole factors permitting the development of marked coronary arteriosclerosis in this case. In short, we have this heart furnishing examples of coronary occlusion without myocardial infarction—symptomless, 'infarction at a distance', and the ætiologic relationship of diabetes mellitus and hypertension to coronary arteriosclerosis.

V. DISCUSSION

Cohnheim and von Schulthess-Rechberg (1881) called the coronaries 'functional end arteries', because clamping them resulted in myocardial infarct. He argued that if there are anastomoses between the two arteries, they must consist of fine capillaries. Gross (1921), after evaluating the evidence, concluded that there are inter-arterial anastomoses both at the capillary and pre-capillary levels. Collateral channels also exist between different branches of each artery. He quoted Pratt's definition of 'end artery' as a vascular structure in which the resistance in the anastomotic circulation is greater than in the parent vessels. Further, Gross pointed out that ordinarily these anastomoses are active and functioning but cannot act as adequate compensatory channels in the event of sudden occlusion of the artery. The irregular margin of the infarct suggested that there is some anastomosis. Wiggers (Levy, 1936) concluded—'from the pathological standpoint, it has long been accepted that coronaries are terminal arteries, for plugged by emboli or thrombi in man or when artificially occluded in animals an infarct results. The rapid necrosis of the heart muscle could scarcely occur were anastomoses present'. Finality has been reached on this most debated issue in the hearts studied by the tinted lead phosphate agar injection technique; no anastomoses are found in normal hearts, whatever the age of the patient. These observations are in accord with Cohnheim's concept of 'functional end arteries'.

The normal anatomic distribution of the coronary arteries is an extremely variable feature. Broadly speaking, however, hearts can be classified into three groups, depending on the relative length of the left circumflex and the right coronary artery. One or the other of these vessels or both may give origin to the posterior descending artery. In group I hearts, the right artery supplies all of the right ventricle, the posterior half of the inter-ventricular septum,

and a large part of the posterior wall of the left ventricle, and terminates as the posterior descending artery. This is also called right coronary preponderant heart. In group II, the left circumflex and the right coronary artery jointly contribute to the origin of the posterior descending artery, and the right and the left coronary supply their own ventricles. This is the balanced circulation group. In group III, the left coronary artery preponderates the heart, the left coronary supplies the whole of the left ventricle and the anterior and the posterior parts of the inter-ventricular septum and also a part of the right ventricle. The significance of the anatomic patterns of the coronary arteries lies in their different susceptibility to the results of occlusions. Blumgart *et al.* (1940) observed that in groups I and II hearts the infarcts are usually healed because of the availability of collateral circulation, whereas in group III hearts they commonly end fatally. These prognostic differences in the three basic anatomic groups of the coronary arteries suggest their clinical significance.

When the coronary arteries are the seat of slowly evolving atherosclerotic process, resulting in narrowing and occlusion dissectable as well as non-dissectable, collaterals develop between the two arteries or between their branches. The pathologic process occluding the vessel may be a thrombus, ruptured atheromatous 'abscess', capillary hæmorrhage into a subintimal plaque or an embolus. Thrombosis on an atheromatous plaque appears to be the commonest occluding mechanism, but careful observations of Horn and Finkelstein (1940) and English and Willis (1943) suggest the intramural capillary hæmorrhage into the plaque precipitates thrombosis in large majority of cases. These morphologic studies have clarified the discrepancies between the pathologic findings and the clinical disease patterns. Levy (1940) says 'advanced disease of the coronary arteries may be present at the autopsy in patients who during life never experienced discomfort referable to the heart'. It is believed that complete occlusion of coronary artery may not be suspected during life and that there may be sclerosis of these vessels out of all proportion to the clinical manifestations. Stroud and Wagner (1941) have drawn attention to 'silent or atypical coronary occlusion'. These peculiarities are explained by the mechanism of inter-coronary artery anastomotic circulation.

There may be complete absence of symptoms if the collateral circulation is adequate. If it is inadequate angina pectoris or myocardial infarction may result, the former if the myocardial anoxia is mild, the latter if the anoxia is severe. Reversible myocardial ischaemia of short or long duration is the physiological basis of both angina pectoris and coronary insufficiency. Infarction, however, is associated with irreversible muscle necrosis.

Functioning anastomoses are important in prognosis. They influence recovery or death in

the event of coronary occlusion. When arterial occlusion occurs gradually, as in atherosclerosis, collateral circulation develops to bridge the gap and serve as a by-pass. These anastomoses may prove perfectly compensatory for reduced vascular supply from the occluded vessel, so that they may well serve the patient for his restricted mode of life. At the present time no clinical methods are available which permit recognition of the vascular distribution in the heart during the life of the patient. However, this may be made possible by the improved methods in diagnostic angiography.

VI. SUMMARY

1. The literature on experimental and technical studies on coronary circulation has been reviewed.

DESCRIPTION OF PLATES

All the figures are reduced to half the actual size. In the line drawings diameter of the vessels has been exaggerated to show morphologic alterations. Common to the 3 plates are the abbreviations LD, LC, RC, C and S which are left descending artery, left circumflex artery, right coronary artery, conus artery and septum that has been removed during the unrolling of the heart.

PLATE I

Figures 1 and 2. Case 2 (A48-37).

Figure 1 is roentgenogram of the injected coronary arteries.

Figure 2 is line drawing of the injected and dissected coronary arteries.

These figures show group III heart, no narrowings or occlusions of the coronary arteries, calcified mitral valve, right ventricular enlargement and anastomotic injection of the conus artery.

A is calcified mitral valve.

PLATE II

Figures 3 and 4. Case 8 (A48-25).

Figure 1 roentgenogram of the injected coronary arteries.

Figure 2 is line drawing of the injected and dissected coronary arteries.

In the figures see group II heart, inter-arterial anastomoses, healed infarct at A, moderate narrowing at B, marked narrowing at O and thrombus at D. Note anastomosis between left descending and conus arteries marked b, b.

PLATE III

Figures 5 and 6. Case 11 (A48-32).

Figure 1 is roentgenogram of the injected coronary arteries.

Figure 2 is line drawing of the injected and dissected coronary arteries.

In these figures are shown group I heart, unilateral injection due to occlusion of the right coronary artery by a thrombus O; absence of infarction anteriorly in the left ventricle with occluded left descending artery at B; fresh infarct at A in the posterior wall of the left ventricle. 'infarct at a distance'; calcification of the right coronary arterial wall at F, calcified plaque at D, and atheromatous abscess at E. Note anastomoses from left circumflex to left descending and right coronary arteries.

2. Schlesinger's technique provides an excellent method for the study of coronary artery pathology. Temperature, pressure and viscosity of the injection mass are standardized. There is no tissue damage so that histological studies can be made to confirm the gross anatomic findings.

3. Hearts studied by the injection plus dissection technique have shown that in the presence of atherosclerotic narrowing or occlusion anastomoses between coronary arteries develop.

4. Clinical disease patterns of coronary artery disease are determined by the adequacy of the anastomotic circulation.

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A Mirror of Hospital Practice

CONGENITAL ABSENCE OF THE UTERUS

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'COMPLETE absence of the uterus, if it ever occurs, is extremely rare, and most cases recorded as such have probably been instances of pseudohermaphroditism' (Eden and Lockyer, 1935).

The case described below is of interest in connection with the statement quoted above.

A young woman, aged 23 years, sought advice at the out-patient department of this hospital for amenorrhœa. She had never menstruated at all in her life. She was married at 15 years of age and began to live with her husband at 17. She was worried because she had not conceived.

On examination, she was a healthy, well-developed and well-proportioned woman with normally formed secondary sexual characteristics: in fact, as fine a specimen of young womanhood as one would like to see.

Locally, the external genitals were normal in appearance and development. On separation of the labia a membrane with transverse rugæ was seen dipping from below the urethral orifice backwards and upwards. At one or two spots a few rugæ were connected with one another by vertical ruckings forming false ostia, which, on tracing with the finger tip and blunt instruments, were found to end blindly. On introduction

symptoms, the only evidence of incompatibility being the poor response to the transfusion, e.g. failure of hæmoglobin to rise.

There is another way in which anti-Rh agglutinins may form, i.e. when an Rh — woman becomes pregnant with an Rh + foetus (the father being Rh +); the foetal agglutinin in this case passes through the placenta and immunizes her. This is potentially more dangerous because the first evidence of it may be a severe hæmolytic reaction following even a first transfusion with Rh + blood. Further complication may arise from the anti-Rh agglutinins in the woman's blood passing back across the placenta and acting on the Rh agglutinin present in the foetus causing hæmolysis and other changes which are the basis of the disorders known as *Erythroblastosis foetalis*. (It is so-called because of the presence of a large number of erythroblasts in the peripheral blood.) There is also a possibility of similar reactions occurring when an Rh — woman who has received repeated transfusions of Rh + blood has a subsequent pregnancy, for the agglutinins or the power to form agglutinins at a short notice may persist in the blood for some years. On the other hand, if there has been hæmolytic disease in an infant, present or previous, it may be assumed that anti-Rh agglutinins are present in the mother's blood and that transfusion may be dangerous to her unless this is done with Rh — blood of suitable group.

Thus we see that Rh — persons may acquire sensitivity to the Rh factor in two ways, (1) in both sexes, by Rh + blood transfusion and (2) in women, after becoming pregnant with Rh + foetus. There is no need for concern at first transfusion into a male or nulliparous female, but when a woman is sensitized by her Rh + baby, the first transfusion may cause an incompatibility reaction. The baby may suffer in its turn from the action of the mother's agglutinins provoked either by its own Rh factor or previous transfusions with Rh + blood. The Rh factor explains why occasional transfusion reactions occur even when the ABO groups are correctly assigned and why it is so important to specially test the blood when multiple transfusions have to be given or when pregnant and puerperal women and new-born children are to be transfused. The safe course is to transfuse an Rh — individual with Rh — blood. But the Rh factor is not a single entity, it is composed of multiple sub-types whose complexities require elaborate investigations if all hazards are to be avoided. In case of urgency, plasma or serum may be used instead of whole blood.

Erythroblastosis foetalis (congenital hæmolytic disease).—There are three forms: (1) the infant may be born dead or moribund with œdema of the body (hydrops foetalis). Many

stillbirths are probably due to the same cause. (2) It may be born jaundiced or develop severe jaundice within 48 hours of birth (icterus gravis neonatorum). (3) Or it may be normal at birth and develop severe anaemia in a few days (congenital anaemia of the new-born). The primary process is destruction of the infant's red cells and the erythroblastosis is merely a response to this destruction. The disease does not occur in all cases of Rh incompatibility, being influenced by several factors, e.g. strength of the antigen in the baby, the extent and type of antibodies formed by the mother, variations in the permeability of the placenta to the passage of the Rh factor and anti-Rh agglutinins, etc. As a result we see many normal babies born of Rh — mothers and Rh + fathers, and variations from baby to baby in the severity of the disease. The first babies usually escape unless transfusion therapy in the mother, independent of pregnancy, has developed the antibodies in her. History of multiple blood transfusions should arouse suspicion, and the discovery of the antibodies in the maternal serum is diagnostic.

Mild cases recover spontaneously, but in others treatment should be prompt with blood transfusion. Rh — blood is used because Rh + cells are rapidly destroyed after transfusion. A donor of group O or the child's own group is selected. The amount of blood transfused should be 10 cc. per pound of body weight and this should be repeated on the second day. When a suitable donor is not available, the mother's blood is a suitable substitute provided it is found compatible by a direct test. The blood cells are first washed (to remove the agglutinins) and resuspended in saline. Results of treatment are disappointing in icterus gravis in which the mortality is still high owing to damage to the cerebral basal nuclei (kernicterus) and the liver. Of those that survive a proportion suffers from neurological sequelæ, e.g. spasticity and mental deficiency. A more promising method of treatment is by 'exchange transfusion', i.e. withdrawal of part of infant's blood with simultaneous replacement by Rh — blood, the exchange being continued until most of the red cells are Rh —. The whole procedure takes 1 to 2 hours, but it can only be done at special centres. For details of the technique see Mollison, Mourant and Race (1948).

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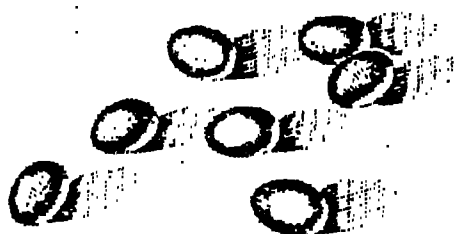
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Indian Medical Gazette

JANUARY

A MARVEL OF HUMAN BRAIN POWER:

HELEN KELLER, LL.D., L.H.D.

Blind-Deaf Author-Educator

THIS prodigy of perception and execution shows that the human brain in most human beings is by no means used to its full capacity. The sensory parts of it can derive their perception even without the aid from eyes and ears, and the motor parts can execute orderly movements like those of speech even from such an incomplete perception.

Born on 27th June, 1880, at Tuscomb, Ala (U.S.A.), Miss Keller had a normal babyhood for 19 months. Then she fell ill and on recovering from the acute stage of the illness was found to be deaf and blind. She became mute also because she had not yet learnt speech except for a few baby words.

For a few years she grew into a half-wild creature and made known her wants by a few noises and gestures only. She went into a rage when not understood. She, however, showed signs of intelligence.

Her people were well off and they sought the best advice available. Alexander Graham Bell, the inventor of the telephone, who was then experimenting with sound, was consulted. On his advice Anne Sullivan, a girl of 20, was taken from the Perkins Institution for the Blind at Boston to train the child now nearly 7 years old. Miss Sullivan herself had become blind as a child and had been cured by an operation. They became inseparable companions until Miss Sullivan died in 1935, leaving behind a friend 50 years old, praying for strength to 'endure the silent dark until she smiles on me again'.

Miss Sullivan had found the child a little savage, irresponsible to coercion or love. In one of the early encounters the pupil knocked out a front tooth of the teacher. Yet Miss Sullivan persisted. The first object introduced to the pupil was a doll. The doll was put in Helen's one hand and its name, *doll*, spelt into the other hand, in the usual finger alphabet. Helen learnt the spelling but did not connect it with the doll. The association between the word spelt and the object felt was not established.

The association developed suddenly on another occasion near an outdoor water pump in operation. The teacher who had taken the pupil out for a walk put one of her little hands under the spout and spelt *w a t e r* into the other hand. The pupil grasped the idea at once and touched the ground to ask its letter-name.

That day the pupil learnt 30 words including 'teacher'. The education had begun. That night affection was also awakened in Helen: She kissed the teacher. The manual of Braille alphabet was soon mastered and Helen was reading and writing.

At 10, Helen desired to speak, having learnt that a deaf and blind girl in Norway had been taught to speak. Miss Sullivan took her to the Horace Mann School for the Deaf in Boston where she received 11 lessons. The lessons were then continued at home by Miss Sullivan. Helen's first sentence spoken to her father and mother was 'I am not dumb'. Certainly she was no longer dumb.

Growing into a young woman Helen wanted to be a university student. After some opposition she was admitted to the Cambridge (Mass.) School for young ladies and later to the Radcliffe College from which she graduated with a Bachelor of Arts degree *cum laude* in 1904. Miss Sullivan attended with her to write into her hand all that she saw and heard. At home Helen wrote in Braille all that had been written into her hand. Her finger tips almost bled at times. Incidentally, Helen has never used her hands for any other work such as knitting.

Even before graduation Helen commenced her literary career. She became an expert typist and wrote serials in journals and books. Her books include: *The Story of My Life* (1902), *Optimism* (1903), *The World I Live In* (1908), *The Story of the Stone Wall*, *Out of the Dark* (1913), *My Religion* (1927), *Midsummer—My Later Life* (1930), *Helen Keller Journal* (1938), *Let Us Have Faith* (1941). She used the Braille typewriter first and then typed the manuscript on an ordinary typewriter. On the use of the ordinary typewriter she possesses a sense not known to us: when she leaves a paragraph or a sentence unfinished, because of an interruption, she returns to it and finishes it without ascertaining the exact place in the interruption!

The teacher got married and the pupil lived with the couple. Later the teacher separated from her husband and lived with the pupil.

Romance came to the pupil also. A young writer who was associated with the public appearances of Miss Keller proposed marriage. The proposal was discouraged by all concerned and the proposer disappeared.

Dr. Keller possesses an extraordinary sense of feeling the vibrations. She enjoys operas and knows the difference between the various classes and compositions. The noise of towns she dislikes and enjoys retreats in the country for the same reason. In 1946, while visiting a London Home for Blind Children, her party could not keep to the schedule and arrived when the children were in bed for their midday rest. While the party was sitting in the reception room and the management apologizing for its inability to alter the routine and get the children out of bed, Dr. Keller spoke and said

'The children are coming'. So they were. She had felt the vibration caused by the little feet. Unknown to the management the routine had been altered and the children were being brought to the reception room. They were, however, too far away for ears to hear.

The 'teacher' herself became blind again and was replaced by a 'companion' Miss Thomson who looked after both the teacher and the pupil. In the photograph are seen Dr. Helen Keller and Miss Polly Thomson. The latter is writing into the hand of the former in finger alphabet. *She can write at the rate of 85 words a minute.* It is not necessary to write them in full. At times Dr. Keller does not want even a sentence to be finished. She takes away her hand to show that she has understood the whole sentence. By her knowledge of previous sentences she knows how a particular sentence would end.

Dr. Helen Keller and her party commenced an Eastern tour last year. In Japan in December 1948 Miss Thomson was declared unfit for medical reasons to continue the journey. The remaining two members of the party, Dr. and Mrs. Milton E. Stauffer, however, continued the journey and arrived in Calcutta early this year. We contacted them through the courtesy of Mr. A. Shah, Principal of the Calcutta Blind School, and Mrs. S. D. S. Greval, President of the Convention of the Teachers for the Deaf and Dumb School, Calcutta. They have supplied the information we are presenting to the readers. For information on the education of the affected children and associated items enquiries will be attended to by: A. Shah, Esq., Principal, The Blind School, Behala, Calcutta; Mrs. S. D. S. Greval, 13/2, Ballygunge Park Road, Ballygunge, Calcutta; and Dr. Milton T. Stauffer, D.D., John Milton Society, 156 Fifth Avenue, New York 10, N.Y. (U.S.A.).

The touring members also supplied us with the following:

1. A photograph of Dr. Helen Keller with Miss Polly Thomson. The photograph was returned after obtaining a copy (*see plate IV*).

2. A letter typed and signed by Dr. Keller. The letter was returned after obtaining a photographic copy (*see plate IV*).

3. Copy of a letter from President Truman to Dr. Keller, wishing her success in her tour through Asia, Middle East and Near East.

4. An announcement by Dr. Keller from Tokyo, cancelling the remainder of her tour and asking Dr. Stauffer to continue.

5. Dr. Keller's message.

6. An address of Dr. Keller at a luncheon of the Board of Directors of the John Milton Society for the Blind, Marble Collegiate Church, New York. At public appearances of Dr. Keller the companion writes into the hand of the doctor who speaks in reply.

7. Two abstracts from one of Dr. Keller's books giving glimpses of her outlook on life, her plaint and her resignation.

Documents 3 to 7 are reproduced below:

The White House,
Washington, D.C.,
Aug. 13th, 1948.

My dear Miss Keller,

I have been informed that you are again travelling through the countries of Asia and the Near and Middle East to continue your work with the blind which has been interrupted by the war. Your tireless efforts to create a better world for the blind of your own country through social legislation, are known to all of us and your concern for the blind in other areas of the world and efforts to help them are among the great humanitarian and cultural contributions.

I know that I speak for the American people in expressing admiration and gratitude to you in this endeavour. In your meeting with peoples of other countries, I know that you will bring courage and comfort to the many who stand in need of your ministry.

May I assure you of my sincere wish for the success of your mission and your safe return home.

Very sincerely yours,
° (Sd.) HARRY S. TRUMAN.

Miss Helen Keller,
c/o United States Political
Advisor for Japan,
Tokyo, Japan.

IMPORTANT

HELEN KELLER CANCELS WORLD TOUR

Miss Helen Keller, internationally known deaf-blind lecturer and author, and her companion Miss Polly Thomson, announced on 24th October, 1948, in Tokyo, Japan, that they are compelled to cancel the remainder of their world tour and return immediately to the United States, due to Miss Thomson's ill health.

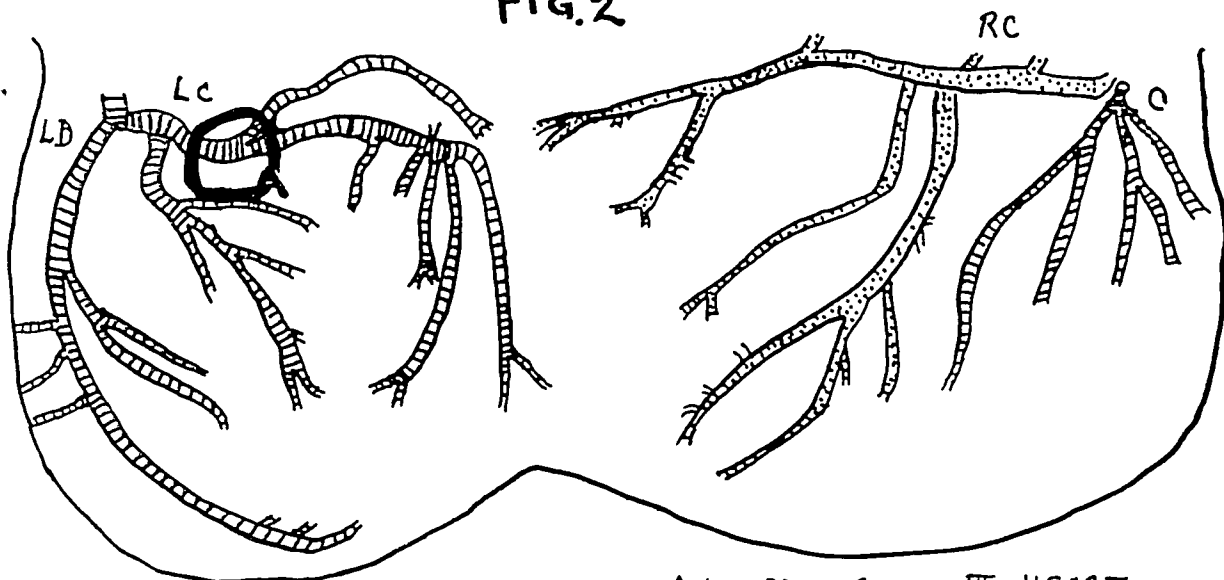
At Miss Keller's earnest request, Dr. Milton T. Stauffer, General Secretary of the John Milton Society for the Blind, under whose auspices Miss Keller and Miss Thomson were to have visited the other countries of the Orient and Near East, will continue the tour as scheduled.

Dr. and Mrs. Stauffer plan to leave Tokyo, Japan, on 30th October by plane for Seoul, Korea, on the first leg of a journey which will take them to China, Siam, India, Pakistan, Iran, Iraq, Syria, Lebanon, Palestine and Egypt. They will carry personal messages to the blind in these countries from Miss Keller, will visit schools, consult with workers among the blind, study conditions and needs as these concern the well-being of the blind.

16 1



FIG. 2



WT 705 Gms

IIIIII BLUE MASS → LT. CORONARY.

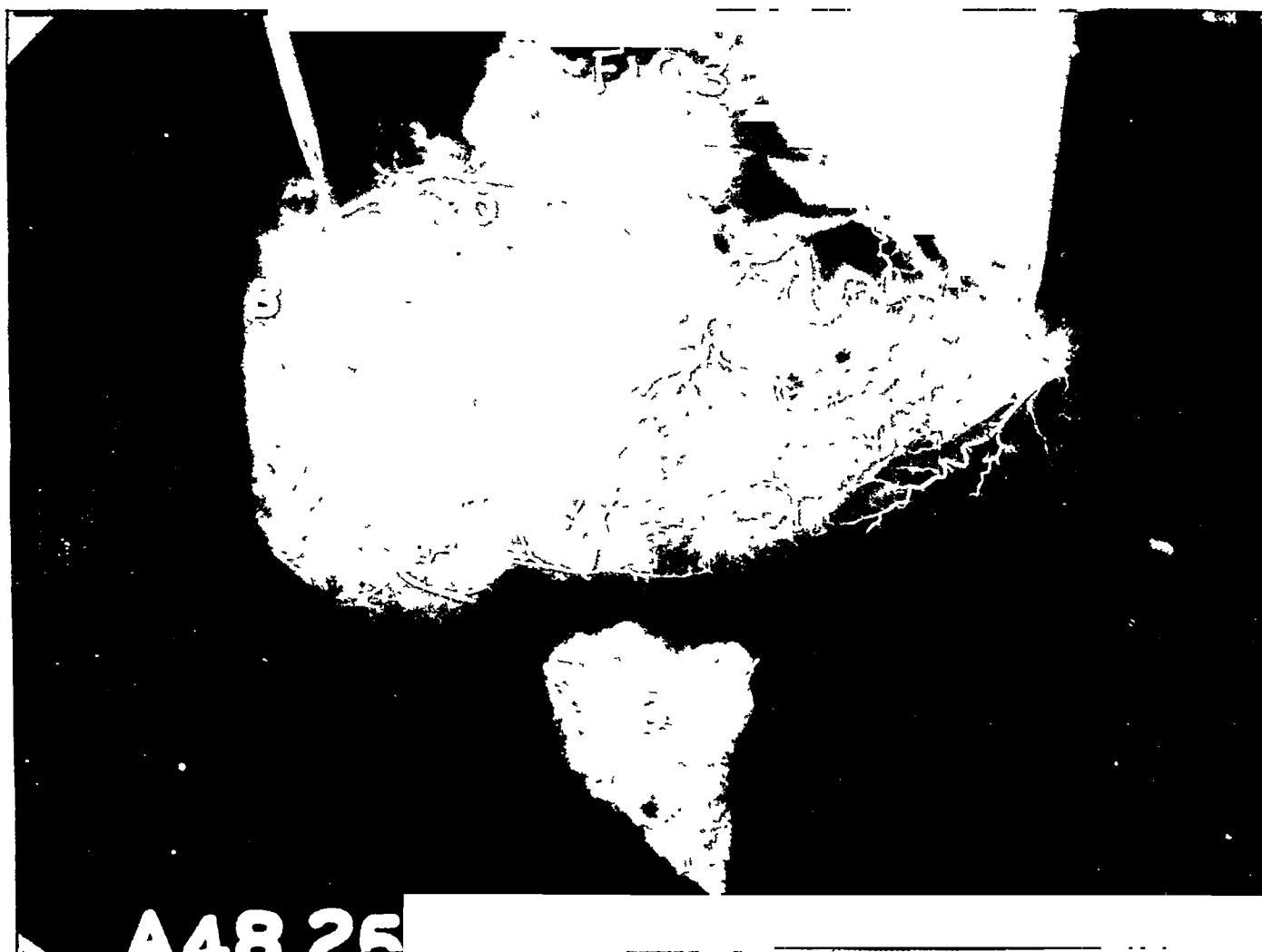
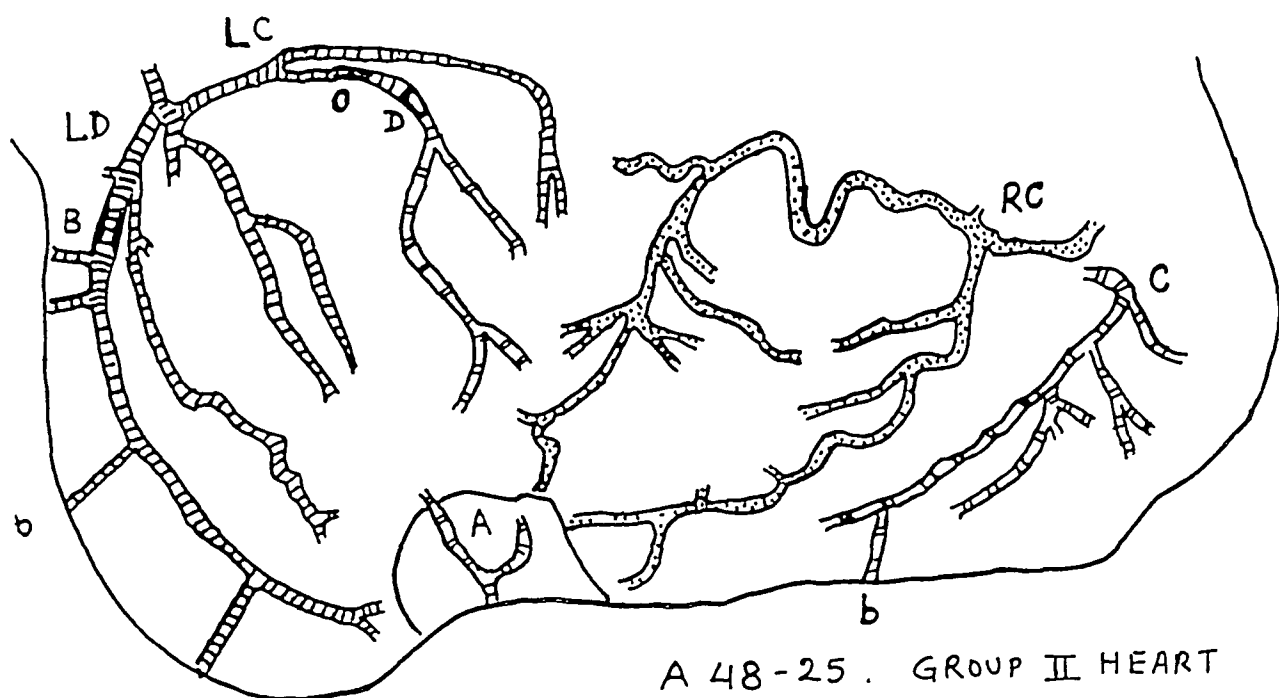


FIG 4



PURPLE MASS
MIXTURE OF RED
AND BLUE

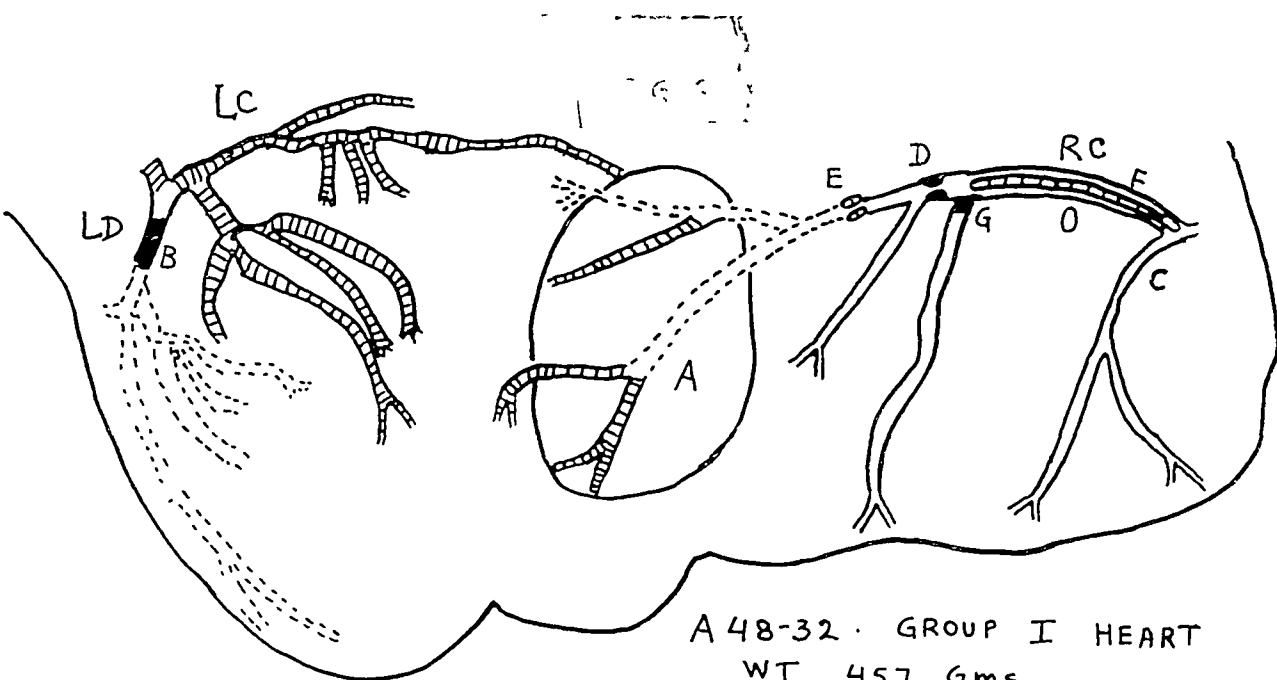
A 48-25. GROUP II HEART
WT 421 GMS.

MASS (RED) INJECTED INTO
RT. CORONARY.

MASS (BLUE) INJECTED INTO
LT. CORONARY.



48 32



A 48-32. GROUP I HEART
WT 457 Gms.

||||| BLUE MASS INJECTED INTO
LT. CORONARY

--- BLUE MASS REACHING BY
ANASTOMOSIS

— NO INJECTION

PLATE IV
A MARVEL OF HUMAN BRAIN POWER : HELEN KELLER. (EDITORIAL.) PAGE 15

93 Seminole Avenue; Forest Hills, L. I., N. Y.,

February 24, 1928

Mr. Lewis B. Chamberlain,
American Bible Society,
New York City.

Dear Mr. Chamberlain,

(I am indeed glad of this opportunity to express my delighted interest in the plan of the John Milton Foundation to increase the supply of embossed religious books for the blind.) I have always known that there is a scarcity of religious literature available for the sightless; but when your letter came, and I looked through the catalogue of braille publications to refresh my memory, I was shocked to find only one or two books that I should consider worth while. (It seems strange to me that so little thought, apparently, has been given to the spiritual needs of the blind.)

The Bible and the writings of Emanuel Swedenborg are almost my only source of religious enlightenment. (The blind especially need books which cultivate the inner vision. What use is it to give them greater material advantages without broadening the life of the spirit?) What good is it to have wider opportunities if they do not bring us the light and the grace that come only with the inner life? The truths of the Bible should be ever burning stars in our darkness. (From my own experience I know how unspeakably precious religion is to those who walk in dark ways, and I am sure the sightless will welcome books which will help them to interpret the Bible in a large, generous spirit.) Of course we have the Bible, and no book can take its place with its combined greatness and simplicity and the wondrous sense it imparts of God's Presence among us; but any book renders us a real service which helps us to discover truths and beauties we have not of ourselves perceived. I sincerely hope the John Milton Foundation will find it possible to supply the blind with the kind of Christian reading that will fructify their minds with faith and cheer their solitude.

With kind greetings and all good wishes, I am,

Cordially yours,

HELEN KELLER

Photograph of a letter typed
and signed by Dr. Keller.



Dr. Helen Keller and Miss Polly Thomson.
Miss Thomson is writing into the hand of Dr. Keller.

HELEN KELLER'S MESSAGE

Dear Friends,

It is a source of profound regret to me that I am not to meet you personally. Long have I looked forward with liveliest pleasure to visiting my handicapped fellows in countries of the Far East, encouraging them to rise above their limitations. It saddens me that this dream must be unfulfilled.

But I have boundless faith in the goodness of the human heart and I am sure that you will respond warmly to the call of the blind and deaf who need your aid to shape their lives anew.

Out of a rich full experience, I know that the blind can be raised from idleness and unhappy dependence to self-help and accomplishment. Your duty in rendering them independent and useful is as much a part of religion as the words of consolation it speaks.

When you see to it that the blind have a chance to do their share in the work of the community, the misfortune of human beings, once without hope, will through you be converted into a wealth of bright possibilities and they themselves will become a precious element among the resources of their country.

Affectionately yours,
(Sd.) HELEN KELLER.

ADDRESS OF MISS HELEN KELLER
at the Luncheon of the Board of Directors of
the John Milton Society for the Blind, Marble
Collegiate Church, New York, 27th January,
1948

Dear Friends,

This is a blessed moment as I foregather with you at the beginning of the greatest venture of my life.

Humbly I rejoice that the Lord has accepted whatever abilities I have for the liberation of the blind of the world from ignorance, beggary and prejudice. It is because I want to share with them my own blessings, that Polly, my like-minded co-worker, and I go forth on our mission under your aegis.

I have only the spoken word—and imperfectly spoken at that, but if God accepted Abel's wee lamb, Moses' staff, the widow's cruse of oil, Dorcas' needle for the good of mankind, I know He will find a new use for my broken speech. And what a wonderful use—to reach the fourteen million blind still waiting in Egyptian darkness for a friend!

With fervent thankfulness I appreciate the warm-hearted manner in which the John Milton Society is inaugurating a programme of services to the blind of the Orient and the Near East, not only to dispel the spiritual fogs that surround them, but also to quicken their intellects and develop their capacities of service to society. That will be the field where I can do my best work, while Dr. Stauffer and others do all they

can to evangelize the blind and provide for their Christian nature.

I am not a teacher nor a preacher. I am just a happy witness to the Light that God sheds upon handicapped human beings throughout the earth. So with Dorcas' needle I reach out to the cold blackness that envelops myriads of human lives, and if I only follow the thread of Divine Love to fulfilment, nothing else matters.

From my heart, I wish you and the Society a happy outcome of your labours that shall include the blind of earth among the multitude who go unto the House of God, their exceeding Joy.

TWO ABSTRACTS FROM
THE STORY OF MY LIFE

For years I have read the Bible with an ever-broadening sense of joy and inspiration; and I love it as I love no other book. The Bible gives me a deep, comforting sense that 'things seen are temporal, and things unseen are eternal' (pp. 112-113).

Sometimes a sense of isolation enfolds me like a cold mist as I sit alone and wait at life's shut gate. Beyond there is light, and music, and sweet companionship; but I may not enter. Fate, silent, pitiless, bars the way. Fain would I question his imperious decree; for my heart is still undisciplined and passionate; but my tongue will not utter the bitter, futile words that rise to my lips, and they fall back into my heart like unshed tears. Silence sits immense upon my soul. Then comes hope with a smile and whispers, 'There is joy in self-forgetfulness'. So I try to make the light in others' eyes my sun, the music in others' ears my symphony, the smile on others' lips my happiness (pp. 130-131).

MEDICAL EDUCATION

It is proposed to publish articles on the above subject as a special feature in a future issue. Contributions in this connection will be received until the 31st March, 1949. Educationists, critics and others are expected to give their best in this important subject.

INDEX FOR I.M.G., VOLUME 83 (1948)

THE index for volume 83 (1948) has been printed and included in the January 1949 issue. Subscribers are requested to detach it and bind it along with volume 83.

ERRATUM

IN the editorial on 'Allergy: Newer Knowledge', I.M.G., 83, p. 568, column 2, lines 9 and 10, for (also local anaphylaxis on a 'prepared' site); not accepted by Schwartzman read (also local anaphylaxis on a 'prepared' site; not accepted by Schwartzman)

Medical News

QUARANTINE NOTICE

(From a note dated 19th January, 1949, issued by the Press Information Bureau, Government of India)

INFORMATION has been received by the Director-General of Health Services that the health authorities in British Somaliland have declared India free from cholera.

RESEARCH WORK IN ATOMIC ENERGY

(From a note dated 20th January, 1949, issued by the Press Information Bureau, Government of India)

THE first conference of the Atomic Energy Commission met to-day at New Delhi to draw up a syllabus for the teaching of nuclear physics, chemistry and mathematics to the University students to equip them for research work in atomic energy.

The conference was attended by Dr. H. J. Bhabha, Dr. S. S. Bhatnagar, Dr. S. N. Bose and Dr. K. S. Krishnan, members of the Atomic Energy Commission and 23 other scientists who represented 14 Indian universities and scientific institutes.

Another meeting of the conference will be held to-morrow to discuss in detail the duration, contents and other questions relating to the syllabus of the abovementioned subjects.

AGRICULTURAL RESEARCH AND SOIL CONSERVATION

I.C.A.R. ADVISORY BOARD CONCLUDES SESSION

A NUMBER of important research schemes including those on improvement of crops, agronomical conditions in general, soil conservation in Himachal Pradesh, setting up a suitable organization for collection of agricultural statistics, research on tuber crops as an aid and substitute for food, standard method for milk analysis and dairy development, were approved by the Advisory Board of the Indian Council of Agricultural Research which concluded its two-day session this month.

The new economic situation in the country consequent upon partition was fully reflected in the Board's deliberations which gave particular emphasis on research schemes in the East Punjab and West Bengal for agricultural rehabilitation. Similarly, the development schemes of Hyderabad and Kashmir came in for special treatment in view of the abnormal conditions prevailing there.

The need for collecting more reliable statistical data on agricultural production was strongly felt by the Board and a five-year co-ordinated scheme of crop cutting experiments of principal crops in various provinces was approved.

A resolution was passed urging upon the Government to sanction more finance for agricultural research as it was felt that to help in making the country self-sufficient in food, wider agricultural research than what limited finances permit at present should be undertaken.

AGRICULTURAL SCHEMES

A soil conservation scheme of the Himachal Pradesh for undertaking an ecological survey, cultivation of soil binders, collection of erosion data and to find out suitable measures to reduce soil losses was recommended. A scheme for the improvement of the soil

conditions in spent-up orchard lands in the Kumaon Hills was another important research item recommended.

TUBER CROPS

The Council had in its previous meetings recommended the cultivation of tubers such as sweet potatoes and cassava as a source of human food, so as to relieve pressure on cereals and had invited Provincial Governments to submit schemes on the subject. Schemes submitted by Bombay, U.P., East Punjab, Bihar, Orissa and Mysore were recommended.

Schemes for the improvement of rice crops in East Punjab, Coorg and West Bengal, and of maize in West Bengal and Bihar were sanctioned. Several research schemes on pulses in Madras, West Bengal, U.P., Bihar, Hyderabad, Orissa, Mysore and Gwalior were approved. Research schemes on millets in Mysore and on palmyra in Madras were also recommended.

A Jaipur Scheme to check soil erosion and spreading of the desert area was approved. The object of the scheme is to prevent the desert from spreading by sand blown by winds, by planting suitable shrubs and grasses which will at the same time provide better fodder for livestock.

A scheme for the co-ordination of research on insect pests and blast and foot diseases of rice in Madras was recommended. An East Punjab Scheme on Wilt disease of gram was also approved. The Council recommended that the animal nutrition scheme of Madras, which was stopped in 1943 due to lack of accommodation for the laboratories, etc., should be revived.

DAIRY DEVELOPMENT

A scheme to explore the possibilities of using milking cows for draught work was considered and approved. It was suggested that the work should be conducted at four centres, including the Indian Dairy Research Institute, Bangalore.

Standardization of the method of analysis of milk and milk products, suggested in a scheme of the Indian Dairy Research Institute, was approved.

After termination of the meeting, the members were entertained to a film show on science and agriculture by Messrs. Patel (India) Ltd.

400 NEW PRODUCTS FROM ONE FIRM

(From Release No. B.F. 76 issued by British Information Services, New Delhi)

WITH manufactures ranging from explosives to plastics and from paints to penicillin, Imperial Chemical Industries have, since 1938, evolved between 300 and 400 new products, the newest addition to the list being 'Antrycide', the new anti-tsetse drug that is likely to revolutionize farming in Africa and which has been described as one of the greatest scientific advances of the age.

It is doubtful whether the work of any other business organization has so benefited mankind, for among the ICI developments announced since the outbreak of war are 'Paludrine', the greatest advance in the fight against malaria, and 'Gammexane', the powerful insecticide. 'Paludrine', besides giving complete protection against malignant malaria, for the first time actually breaks the cycle of malarial infection, while 'Gammexane', although possessing 15 times the strength of DDT, is no more toxic to human beings than aspirin.

'Methoxane', the selective weed-killer that does no harm to growing crops, is another ICI discovery of recent years. This British chemical group was also responsible for the development of 'Polythene' which made possible the rapid development of radar, and 'Perspex', another important factor in the Allied air strength.

'Ardil', wool-like fibre from groundnuts, 'Vynide', new type of leather cloth, and 'Alcian Blue', the world's first bright turquoise dye that is fast to both light and washing, are other ICI developments.

ATOMIC ENERGY AIDS MEDICAL RESEARCH

(From Release No. B.F. 58 issued by British Information Services, New Delhi)

Atomic energy is not a dream of the future but is already being applied extensively to constructive ends, such as medical research. This is the view of Sir John Cockcroft, Director of the British Government's Nuclear Research Establishment at Harwell.

By using radio-active iodine, it is possible to see where the iodine is going in the treatment of the thyroid gland, while radio-active phosphorus can be used to test how food is utilized in the body, as well as to check the volume of the blood.

In the oil industry, a little radio-active carbon, if introduced into crude oil, enables it to be followed in its wanderings round the chemical plant. Metallurgists are interested in the rate at which bearings are being worn and it will be easy to study this and the effects of various kinds of lubricants.

Radio-active tracer elements are now being used for the study of plant growth also. By mixing radio-active atoms of phosphates with ordinary fertilizers, it is possible to see how a plant uses the fertilizer with which it is fed. By mixing radio-active carbon dioxide with ordinary carbon dioxide, the method by which plants

turn carbon dioxide into food under the influence of sunlight can be studied.

Sir John believed that within three or four years small experimental units would be using nuclear power for industrial purposes. There were a number of problems which were presenting a real challenge to engineers, metallurgists, physicists and chemists. 'We must not expect nuclear energy to contribute anything appreciable to world power during the next 10 years, but there is a good prospect that in time it will take its place alongside other sources of power for the benefit of mankind'.

INAUGURATION OF FIRST CO-OPERATIVE HEALTH CENTRE

THE Hon'ble Rajkumari Amrit Kaur, Health Minister, Government of India, performed the opening ceremony of the first of a series of six Co-operative Health Centres planned for Delhi by the Ministry of Relief and Rehabilitation, at Diaz Square compound (between Gole Market and Ibbetson Road, New Delhi) on Wednesday, 5th January, 1949, at 5-15 p.m.

In all 10 Co-operative Health Clinics are proposed to be opened under a scheme drawn up by the Relief and Rehabilitation Ministry. Six of these will be Allopathic, two Homœopathic and two Ayurvedic. Allopathic Centres will be located at Gole Market, Faiz Bazar, Babar Road Colony and Lodi Road Colony. One Allopathic, Homœopathic and Ayurvedic Clinic each will be located at Sabzi Mandi and Northern Extension Colony.

Medical Councils

WEST BENGAL COUNCIL OF MEDICAL REGISTRATION

ABSTRACT OF IMPORTANT ITEMS OF THE MINUTES OF THE MEETING HELD ON 10TH AUGUST, 1948

1. THE following resolution which was passed by the Madras Medical Council at their meeting in March 1948, was adopted :—

'That the primary registration of basic qualification should be in the Register of the Council in whose jurisdiction the University or Examining Body is situated.'

2. The Council directed the removal of the name of a practitioner from the Register under section 25(a) of the Bengal Medical Act for having participated in the dispensing of a prescription which had 5 grains of quinine, by giving only 0.71 grains.

3. The Council directed the removal of the name of a practitioner from the Register under section 25(a) of the Bengal Medical Act for giving untrue and improper certificates.

4. Two practitioners had given misleading Yellow Fever inoculation certificates. The Council warned them and required them to submit in the first week of July 1949, certificates from two registered practitioners of their professional conduct, the final order being kept pending till the meeting of the Council in August 1949.

5. The Council recommended to Government the recognition of the M.B.B.S. degree of the Agra University as a qualification registrable under the Bengal Medical Act, 1914, and the amendment of the Schedule to the Act accordingly.

MINUTES OF THE MEETING OF THE UNITED PROVINCES MEDICAL COUNCIL HELD AT LUCKNOW ON SATURDAY, 20TH NOVEMBER, 1948

1. The minutes of the last meeting were confirmed.
2. Government notifications about the election and nomination of some members were read and recorded.
3. The Registrar's annotations on the audit and inspection note on the accounts of the Council for the year 1947-48 were approved and the amount to be recovered from Captain Goldblum was written off.
4. The statement of income and expenditure of the Council for the year 1947-48 was approved and sanction was accorded to excess expenditure, over budgeted allotments, under certain heads.
5. The budget estimates of the Council for the year 1949-50 and the revised budget for the year 1948-49 were passed unanimously.
6. The case against Dr. Pran Nath Seth was considered and it was unanimously decided that the case against Dr. Seth be closed.
7. The case against Dr. Harkishan Singh Ahlowalya was considered and, after hearing him and his two witnesses, the Council unanimously found him guilty and directed the Registrar to remove his name from the medical register. It was further unanimously carried that he may be permitted to apply (with necessary certificates) for restoration of his name after a period of two years.
8. The case against Dr. Shyam Behari Lal Srivastava was considered and, after hearing Dr. Srivastava who expressed unqualified regret for his mistake, the Council

found him guilty, but in view of his expression of regret, unanimously decided that he may only be warned this time.

9. Resolved that this Council was in agreement with the following resolution of the Madras Medical Council and that they may be informed accordingly.—

'That the primary registration of basic qualification should be in the register of the Council in whose jurisdiction the University or Examining Body is situated.'

10. Resolutions nos. 12 and 15, passed at the Provincial Medical Conference of the All-India Medical Licentiates' Association held at Moradabad in April 1948, were talked out.

11. The registration of Dr. Harbans Singh was confirmed.

12. The orders of the President permitting the registration on payment of Rs. 5 only of practitioners who were registered in the United Punjab, but have not been registered by the East Punjab Medical Council, were confirmed and it was agreed to that the reciprocity of free registration which existed with the United Punjab Medical Council should now be extended. East Punjab Medical Council provided the Government reciprocates.

It was given by Dr. Jagdish Prasad to file and the Council directed that his name be drawn to section 28 of the United Provinces Medical Act of which a copy may be forwarded to him.

The recommendations of the Standing Committee were accepted and it was further decided that the Council of the Indian Medical Association may supply of Council's notifications was not obligatory under the provision of the United Provinces Medical Act, or under the rules, and that the notifications and orders are supplied for information as a matter of courtesy which the Council have assured themselves, reference to the records, has been uniformly made to his association.

The sitting members of the Standing Committee were unanimously re-elected for the year 1949.

16. Resolved that Dr. Sudhir Chandra Ghose should get his name restored to the Bihar Medical register.

17. Government endorsement directing this Council to act according to the suggestions of the Medical Council of India was noted. Further, it was decided to move the Government to cancel their notification no. 750-V-163, dated 24th April, 1930.

18. Resolved that the draft Bill to regulate couching be approved and submitted to Government for further action.

19. Resolved that the amendments to the Indian Medical Degrees Act as tentatively communicated by the President in his letter, dated 28th July, 1949, be approved.

20. Resolved that the Government be moved to cancel reciprocity of free registration in respect of those provinces which are now outside the Indian Union.

21, 22, 23 and 24 Disposed off under item no. 14 supra.

25. Withdrawn.

A. C. BANERJEA,
President, Medical Council,
United Provinces

R. N. SHUKLA,
Registrar.

The Indian Medical Gazette Fifty Years Ago

LONDON LETTER

(Reproduced from the *Indian Medical Gazette*,
Vol. 34, January 1899, p. 20)

The Plague in Vienna

THE outbreak of plague which took place at Vienna last month has attracted great attention. It appears that the Austrian Commission which visited Bombay last year for the purpose of investigating plague brought back with them cultivations of the bacillus with which sundry experiments have been made. The organism has been kept in an active condition, and a laboratory attendant named Barisch somehow—probably from incautious handling of the material while in a state of intoxication—inhaled some of it and took ill with symptoms of pneumonia on the 5th of October. Cultivations from the sputum and inoculation of rats with the same were made and at first gave negative results, but eventually typical colonies of the plague bacillus were produced both from sputum and from the blood of one of the inoculated rats. Barisch died on the 18th of October. He was attended by Dr. Mueller, who sickened on the 21st of October, and died the next night. A nurse, named Peeha, contracted the disease on the 20th, and died on the 30th. Elaborate isolation and disinfection precautions were adopted, and up to the present time no further case has occurred. The outbreak may, therefore, be considered to be at an end, but it has aroused a fresh interest in the subject of plague.

Indian Plague Commission

A Special Commission has been appointed in this country to inquire into the origin of the various outbreaks of plague which have taken place in India during the last two years; and the manner in which the disease is spread. The Commission has also been instructed to investigate the subjects of the serum treatment and prophylactic inoculation, and to express an opinion on the efficacy of both these procedures, and to advise on the general question of prevention. Dr. T. R. Fraser, Professor of Materia Medica and Clinical Medicine in the University of Edinburgh, has been appointed President. A better choice could not have been made. researches regarding the antagonism of the physiological and therapeutic act of streptococcus and the treatment of snake-antivenene indicate his special aptitude. The Commission has been charged.

to be a man of great general ability, genial disposition and sound judgment. Two scientific men of established reputations, namely, Professor A. E. Wright of the Army Medical School, Netley, and Dr. M. A. Ruffer, President of the Sanitary Maritime and Quarantine Council, Alexandria, have been appointed members; and two Indian civilians, Messrs. J. P. Hewett and A. Cumine, will be associated with them, and supply the knowledge of administrative and social conditions in India, which is so necessary to take into consideration in formulating recommendations regarding preventive measures. The composition of the Commission is thus admirably conceived, and will bring to bear upon plague problems high scientific capacity and an unbiased mind, while the civilian element will restrain and guide its deliberation in respect of those delicate questions into which the special sensibilities and prejudices of Indian populations enter. The time allotted for the work, namely five or six months, will not permit of much original research being done; but there is in existence a very large body of evidence, clinical and pathological, relating to plague which will be collected and sifted, and an authoritative pronouncement may reasonably be expected on many points, which remain at present obscure and unsettled.

The Soudan Expedition and Egyptian Insanitation

Lord Kitchener of Khartoum is enjoying a triumphal progress through England; the Fashoda trouble has been set at rest by the withdrawal of Major Marchand and his heroic followers; the song of praise of the Nile campaign has been loudly sung during the last two months, and the changes have been rung on the masterly conception of the undertaking and its consummate execution on the bravery of the troops—British and Egyptian—engaged in it; on the advantages to civilization and commerce which will accrue in consequence of the rescue of the Soudan from the cruel tyranny of the Khalifa; on the economy of the expedition and the material benefits which have been already attained by it; on the skill and industry of the engineers and railway constructors who first paved the way for conquest and then opened the Nile valley for trade; on the efficiency of the medical arrangements and the thoroughness with which the agencies charged with transport and supply fulfilled their important tasks. These things represent the bright side of the picture; but there is a dark side. Although the British troops employed in the Soudan were withdrawn with the utmost possible expedition, they suffered severely from diarrhoea, dysentery and enteric fever of a very virulent type. The same experience was met with in the Dongola

Expedition of 1896 during which in addition a smart outbreak of cholera occurred. The admissions from enteric fever on that occasion amounted to seven, and the death to 3.48 per cent of strength, the case mortality being 50 per cent. Lieutenant-Colonel Sloggett, R.A.M.C., whose report on the medical transactions of this expedition is published as an appendix to the last report of the Army Medical Department, remarks on the serious type of the enteric fever which caused such a high death rate. There is no station in which British troops serve in which the sickness and mortality rates of enteric fever are so high as Egypt, and the experience of these two expeditions indicate that the causes, which produce the result in Lower Egypt, are equally rife throughout the whole of the Nile valley if not more so. Egyptian sanitation is still in a very backward state, and that of the inhabited places bordering the Nile is evidently no better if not worse. Whether these bowel complaints and fevers are caused by contamination of air, water or soil or by impurity of all three is a difficult question; but the British occupation of Egypt is attended by a lamentable loss of health and life from conditions which are considered and with reason to be capable of prevention, and the sanitary question must sooner or later be seriously tackled—the sooner the better.

Criminal Abortion in India

The sentence of death which was recently passed on a medical man convicted of committing the crime of procuring abortion is a notable circumstance. The sentence has been commuted; but the fact that it was pronounced, marks with terrible gravity the serious character of the crime. This is the second notorious case in which a severe punishment has been meted for the perpetration of the offence; and public feeling has been roused in view of the frequency, immorality, and danger of foeticide. It cannot be too loudly proclaimed that any medical man who allows himself to be drawn into practices of the kind, whether the result be fatal or not commits an act which is not only criminal and wrong, but is also opposed to every proper professional instinct and inconsistent with the motives and traditions which constitute the basis of professional ethics and honour. I am afraid that in India inducements to procuring abortion criminally are frequent and strong, and I have known instances in which solicitations in that direction have caused medical men to swerve from the path of rectitude; but apart from considerations of personal reputation and professional honour, the blunt truth should never be forgotten that foeticide is murder, and, if fatal to the unfortunate mother, double murder.

10th November, 1898.

Current Topics, Etc.

New Methods of Therapy in Cirrhosis of the Liver

By LESTER M. MORRISON

(Abstracted from the *Journal of the American Medical Association*, Vol. 134, 1947, p. 673)

METHODS OF TREATMENT

THE treatment which the author has adopted consists in the administration of methionine, 2 gm. daily; choline chloride, 2 gm. daily, a special liver extract prepared by the filtration and concentration of an aqueous liver solution containing vitamin B complex; a high protein (higher than heretofore advocated), low fat, moderate carbohydrate diet and frequent feedings of skimmed milk.

This therapeutic regimen was adopted for two reasons: first, as is now well known, the experimental evidence obtained in animals indicates conclusively that choline and methionine are proven lipotropic agents in the prevention and alleviation of fatty cirrhosis of the liver in the experimental animal. The experimental evidence that has been amassed in cirrhosis of the liver and in cirrhosis due to alcoholism in human subjects indicates that cirrhosis is a form of nutritional deficiency disease, or, more specifically, a liable methyl-group deficiency disease. It is also possible that cirrhosis of the liver may be due to a specific vitamin deficiency, just as the macrocytic anaemia of pernicious anaemia and sprue appears now to respond specifically to folic acid therapy.

Second, in a controlled series of 62 patients over an eight-year period, therapeutic results suggested that the combination of methionine and choline resulted in a better therapeutic response than did various other combinations of amino acids, diet, liver- and vitamin supplements in the treatment of hepatic cirrhosis.

A special liver extract was used because of experimental evidence that indicated its importance, when used with choline derivatives, as an aid in the prevention of hepatic damage. In addition, clinical evidence showed that a crude liver extract has definite therapeutic value in the treatment of human cirrhosis of the liver. The author used a specially filtered liver extract fortified with vitamin B complex, the administration of which was relatively painless, thus allowing large quantities (3 to 5 cc.) to be injected intramuscularly daily, or every other day, for periods varying from several weeks to several months; injections were tapered off to twice or once a week depending on clinical and laboratory progress in each case.

The high protein diet which prescribed consisted not only of a high casein source of proteins by the use of skimmed milk feedings and cottage cheese but also of servings of meat three times a day wherever possible. The importance of a high protein diet in cirrhosis of the liver is now thoroughly established and takes precedence over dietary carbohydrate in therapeutic importance. The maximum use of meat in this diet appeared to be advisable because of the necessity for providing the essential amino acids which contain the basic methyl groups, with and without the sulphur radical. These methyl groups are required by the liver for the transmethylation function which institutes regeneration and healing in cirrhosis.

In all possible ways, in cases in which the patient could tolerate it, the patient's diet was stepped up to the limits of tolerance by forced feedings, or any other device, in the attempt to ingest the ideal maximum intake of 200 to 300 gm. of protein, 300 gm. of carbohydrate and 50 gm. of fat.

CLINICAL MATERIAL

A group of 20 patients with proved cirrhosis of the liver were treated and diagnostically divided into (a) 9 patients with ascites and (b) 11 patients apparently free of ascites. All 20 patients revealed characteristic physical signs and symptoms of cirrhosis of the liver.

The ages ranged from 36 to 64 years, with a group average of 50 years. The average duration of symptoms on presentation for treatment in the group was 1.6 years, with a range of from one month to five years. For comparison a control group of 23 patients with cirrhosis of the liver was analysed.

Improvement was measured both in clinical terms, such as decrease in the size of the liver, increase in strength and appetite and amelioration of pre-existing symptoms, together with improvement toward normal values in liver function tests. The tests were found to be valuable index of clinical improvement when clinically interpreted in the knowledge of their limitations and usefulness.

The Treatment of Shock by Aortic Transfusion during Thoracic Operations

By E. B. KAY

and

V. D. HACKER

(Abstracted from the *Journal of the American Medical Association*, Vol. 134, 14th June, 1947, p. 604)

ARTERIAL transfusions may have occasional value in thoracic surgery. Uncontrollable haemorrhage during thoracic operations is a potential hazard. If this complication should occur it may be impossible to provide sufficient blood intravenously after haemostasis to sustain life. It may be difficult or occasionally impossible to obtain veins for venipuncture if the patient is in shock. Unnecessary time may be lost in attempting venipuncture. Even though blood can be provided in adequate amounts the dangers of pulmonary oedema and right sided cardiac failure are ever present when blood is given too rapidly intravenously.

The mortality rate from injuries of the mediastinal vessels is high. Though the haemorrhage may be surgically controlled, death may result from loss of blood and shock. If the state of shock persists unduly long permanent damage may result from anoxaemia of the brain, kidneys and liver. Heretofore, treatment has consisted mainly of intravenous replacement and cardiorespiratory stimulants. The aorta lends itself readily for the administration of blood as an emergency procedure during operations within the chest. Furthermore, oxygenated blood can be provided, thus reducing the factor of anoxaemia. The following case report demonstrates the benefit possible from such a procedure.

REPORT OF CASE

At 3 o'clock in the morning of 16th November, 1946, a Negro man, aged 60, was admitted to the accident room of St. Luke's Hospital. He was semi-conscious, inebriated and in shock. He had received a stab wound in the first intercostal space adjacent to the sternum approximately thirty minutes prior to entry. The pulse was feeble and soon disappeared. The blood pressure was unobtainable. The right side of the chest was dull to percussion. Faint breath sounds could be heard anteriorly near the sternum. There was evidence of a mediastinal shift to the left. Fluoroscopic examination revealed the right chest to be opaque and the mediastinum shifted to the left. Plasma was given immediately without significant benefit; this was followed by a blood transfusion. Though the blood pressure and pulse were unobtainable the patient continued to have rapid gasping respirations. From the position of the stab wound it

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was felt that the innominate artery or the superior vena cava had been injured.

He was taken to the operating room and a thoracotomy performed. As a result of the profound shock and alcoholic consumption it was possible to introduce an intratracheal tube under light anaesthesia. Controlled ventilation was maintained by the anaesthetist during the operative procedure, mainly with oxygen.

The right side of the chest was entered anteriorly through the bed of the second rib. The sternum was transected to allow adequate exposure of the superior mediastinal vessels. There was no bleeding from the wall of the chest when the incision was made. It was noted that the internal mammary artery had been severed approximately 1 inch (2.5 cm.) from its origin by the injury. Blood was slowly oozing from the cut section. This artery was immediately ligated. The entire right side of the chest was filled with clotted and fluid blood, which was removed. No other source of bleeding from the mediastinal vessels or from the right lung could be found. The patient still had no pulse or blood pressure, and the heart was observed to be beating rather slowly, as in failure. As an emergency procedure an oxygenated transfusion was given into the ascending aorta through a size 18-needle. The first portion of the transfusion was given by oxygen pressure and the latter by pressure from a hand pump. Five hundred cubic centimetres of blood were given in three minutes. There was no bleeding from the aorta after the removal of the needle. Immediately following the aortic transfusion a pulse was palpable, and as the chest wall was closed the blood pressure was 80 systolic and 50 diastolic.

The post-operative course was characterized by drowsiness, diarrhoea and incontinence for the first three days. It was impossible to determine the urinary output during this time. There was no urinary output on the fourth and fifth post-operative day, while the daily fluid intake was 3,000 cc.

Chemical analysis of the blood on the fourth post-operative day showed the non-protein nitrogen to be 182 mg. per hundred cubic centimetres, the creatinine 14.1 mg. per hundred cubic centimetres and the carbon dioxide combining power 36.2 volumes per cent. The serum protein level was 6.8 gm., the chlorides 554 mg. and the sugar 141 mg. per hundred cubic centimetres. The non-protein nitrogen increased to 219 mg. per hundred cubic centimetres on the seventh post-operative day.

It was felt that the renal damage and failure were probably due to anoxaemia of the kidneys during the period of shock. The possibilities of previous renal disease and of reaction to transfusion were also considered. Appropriate treatment was administered for the renal failure. On the sixth post-operative day the urinary output was 670 cc. and the amount increased daily thereafter. The non-protein nitrogen and blood creatinine values gradually decreased, so that at the time of discharge on 7th December, 1946, the non-protein nitrogen was 45.5 mg. and the creatinine 1.8 mg. per hundred cubic centimetres. Urine analysis six days post-operatively showed a concentration of 1.015, a trace of albumin, and an infrequent red blood cell but no cast. Subsequent microscopic analyses of the urine revealed no abnormalities.

A check-up examination on 22nd January, 1947, showed the patient to be in good health and asymptomatic except for paresthesia in both hands. A urea clearance test at this time was 68 and 74 per cent of normal.

Vaccination Against Smallpox

By R. SPAETH

(Abstracted from the *Journal of the American Medical Association*, Vol. 134, 14th June, 1947, p. 625)

It is significant that a number of simple, yet very important, details are not common knowledge among the public and the medical profession.

In private practice the matter of dressings is a constant source of discussion between physician and patient or parent of the child to be vaccinated. Considerable conservation of time and avoidance of misunderstanding can be effected by placing a plain band-aid over the insert immediately after vaccination. In my experience no harm can come from such a type of dressing. This may be removed the following day, and further dressings need not be used. However, with the appearance of the vesicle (about the fourth day) daily application of 3 per cent picric acid solution in medicated ('rubbing') alcohol produces a hard, resistant vesicle. To quote the original source of this information (Ratner, Bret: *Allergy, Anaphylaxis and Immunotherapy, Basic Principles and Practice*, Baltimore, Williams and Wilkins Company, 1943, p. 271), 'Much or all of the difficulty of the subsequent care of the vaccination can be prevented by daily application to the vesicle of a 3 per cent picric acid solution in medicated alcohol. This produces a hard, resistant vesicle. The child can be bathed throughout the period of vesiculation and pustulation. Secondary infection is minimized, no protection is needed, scarring is lessened because of the smaller degree of pustulation and finally itching is reduced. There is no interference in any way with successful vaccination. I have used this method for the past twenty years with complete satisfaction, after having read about its use by a medical army officer in some journal which reference I cannot recall. Schamberg and Kolmer (1911) also report on this method, advising the use of 4 per cent picric acid solution in 70 per cent alcohol'. I have observed the formation of a hard, resistant vesicle within twelve to twenty-four hours after several applications of 3 per cent solution in medicated ('rubbing') alcohol, and the parents have unanimously praised the procedure.

Since occasional instances of post-vaccinal tetanus have been reported, every effort should be made to immunize infants and children against the disease (tetanus) preceding vaccination. It is therefore pertinent, that the alum precipitated toxoid can be given at intervals of three to four weeks (instead of three months) without interfering with the development of adequate immunity (to be published later). Hence the present nation-wide urge toward vaccination against smallpox can be utilized to immunize against tetanus (alone or against diphtheria simultaneously by the use of diphtheria-tetanus toxoid). Obviously, the absence of immunity against tetanus should not deter the physician from vaccinating, particularly if the picric acid solution (as described) is employed.

The selection and preparation of the site for vaccination justify comment. The use of the deltoid region is safer than the lower extremity (less likelihood of infection). With the multiple pressure technique, using a very small insert, supplemented by the use of the picric acid solution in alcohol, the problem of disfiguring scars may be dismissed. The best technique is described by Ratner (*see previous reference*): 'The skin of the upper arm in the region of the depression formed by the insertion of the deltoid muscle should be gently but thoroughly cleansed with acetone on sterile gauze or cotton and wiped or allowed to dry a few seconds. Acetone is suggested as a cleansing agent rather than alcohol for the following reasons: (1) It is a more efficient cleanser. (2) It is cheaper. (3) It is not denatured with substances which may possibly affect the vaccination result. (4) It evaporates more rapidly. (5) Approximately 200 vaccinations performed after the use of acetone and alcohol on alternate subjects resulted in more successful vaccinations with acetone than with alcohol'.

Most patients or parents find it difficult to understand the course of vaccination (no immunity, partial immunity, complete immunity and unsuccessful). Verbal descriptions leave them more confused than enlightened. Consequently a coloured description of the various types of take is of value. A good example may be found in Holt and McIntosh's textbook of paediatrics. I have used this for instruction in my office and have

found it invaluable. It would be very helpful to have an office form describing the various types of local reaction so that parents could determine whether or not the vaccinations have pursued a proper course.

A word of caution is indicated concerning constitutional reactions to vaccination. The appearance of fever and associated complaints with the appearance of the pustule may or may not be caused by the vaccination. I can recall several instances in which constitutional complaints at the time of the pustulation were caused by other diseases (e.g. influenza bacillus, meningitis, membranous tonsillitis).

It is commonly believed (at least by the public) that failure of repeated attempts at vaccination indicated immunity. Obviously this belief is an error. Sir William Osler could not be vaccinated successfully but developed smallpox following clinical exposure.

New Concepts in the Treatment of Relapsing Malaria

By J. J. SAPERO

(Abstracted from the *American Journal of Tropical Medicine*, Vol. 27, May 1947, p. 271)

It has been pointed out that despite the magnificent contributions of wartime research towards the producing of new and more efficacious antimalarial drugs, the ideal drug capable of radical cure remains to be discovered. This means that the practising physician must continue to deal with antimalaria agents known to be of sub-optimal efficacy—that ways and means must be devised of attaining the best possible effects from drugs only partially effective in overcoming the notorious relapsing tendency of malarial infections.

Attempts to discover the most efficacious scheme of treatment however have in the past led to much confusion and controversy. This is to be expected for, frequently, identical therapeutic schemes, when repeated on different groups, have produced amazingly different results.

The objective has been to examine the probable underlying causes which have led to discrepancies and confusion in therapeutic evaluation.

To emphasize the major factors which seem to be concerned, a formula of radical cure has been devised. The formula states that the probability of radical cure in an individual, or of cures in a group is determined by the effectiveness attained by the factor of host immunity. The net effect of these in turn is reduced or augmented by a third factor, the inherent characteristics of the species or strains of malaria concerned.

The formula is not intended as a precise statistical method which will determine the likelihood of cure. Rather it purports to express the broad and general principles which are concerned in the mechanism of cure. Its workings for illustrative purposes, however, may be demonstrated arithmetically. For example if inadequate treatment, roughly of 25 per cent effectiveness is given, and if immune response similarly is about 25 per cent the net result of these two factors alone would give about 50 per cent cures. This percentage, however, when multiplied by the third factor, might be either doubled or halved. Thus 100 per cent cures might still follow if the strain concerned were drug susceptible, or there might be only 25 per cent cures, if the strain were inherently drug resistant. This suggests how variably the mechanism of cure may operate to produce almost any given curative result.

The formula emphasizes: (a) That results achieved by any given system of treatment may be dominated by factors quite independent of the treatment itself; (b) if identical regimens of treatment are employed in different groups, variable results are inevitable, for only by coincidence could either of the other two factors operate in an identical manner; (c) that, as a result,

divergent results which follow in trials evaluating treatment actually should not be confusing but are to be expected; and finally, (d) that the common recourse which is so often taken when a plan of treatment fails, such as doubling or prolonging dosage or otherwise revising standard forms of treatment, should be undertaken only when one is convinced that the true explanation of failure does not rest in the operation of other equally influential factors.

Finally, a full consideration of the problem of preventing reactivation seems to demand not only the broader concepts which the formula suggests, but in addition, an understanding of many newer concepts by which each of the various factors in the formula tend to express themselves. Among the most important of these is the postulate that an exo-erythrocytic cycle exists in man; and the corollary, that two types of reactivation occur; exo-erythrocytic (relapses) as well as erythrocytic (recrudescences). In regard to therapy which aims at radical cure, the use of drugs capable of both exo-erythrocytic and erythrocytic activity appears to be essential. In regard to immunity sporozoite dosage looms as of new interest and of great importance is the pattern of clinical activity in the human host. Drug susceptibility and the pattern of relapse appear to be the essential elements peculiar to species or strains of species which are important in determining whether cure or clinical reactivity will follow.

These are matters, then, that constitute new concepts which in turn promise to provide a more rational and better understanding of the many difficult problems involved in the treatment of relapsing malaria.

Post-Operative Convalescence

By HEDLEY ATKINS

(Abstracted from the *Practitioner*, Vol. 159, August 1947, p. 87)

FOWLER POSITION

ON 1st March, 1900, George Ryerson Fowler read a paper before the Brooklyn Surgical Society advocating the raising of the head of the bed by fifteen inches in cases of peritonitis in order to localize infected material to the pelvis. Mayo Robson and Moynihan in this country elaborated this idea, and propped such patients up with pillows so that the trunk was at an angle of 70° to the bed and he was supported by means of a 'donkey' under the knees. This came to be known as 'the Fowler position' and its use was extended, not only to cases of peritonitis, but virtually to all patients in the post-operative phase who could be so positioned without danger. In 1946, Spalding astounded the surgical world by a wholesale condemnation of the Fowler position, and opinion has hardly had time to settle after the shock it received.

The Fowler position was originally introduced in order to localize intraperitoneal fluids to the pelvis and it had no other purpose. Since then, however, its advocates have claimed that it allows better ventilation of the lungs, an unembarrassed action of the heart and more physiological function of the digestive tract. But we must observe that the maintenance of the Fowler position requires constant supervision, otherwise the patient 'slumps'; it is not in fact the position which the patient instinctively chooses, he tries to wriggle down into bed and if we are going to take steps to counteract his instincts, we must be very sure of our ground.

First let us consider the question of localization of peritoneal exudate to the pelvis. Although it is allowed that for fluids and soluble toxins the pelvic peritoneum is equally as absorptive as the rest of the peritoneum, and toxæmia therefore is as severe with pelvic collections as with collections elsewhere, nevertheless, the aim is to localize pus so far as possible to the pelvis because pelvic abscesses are easy to deal with, whereas

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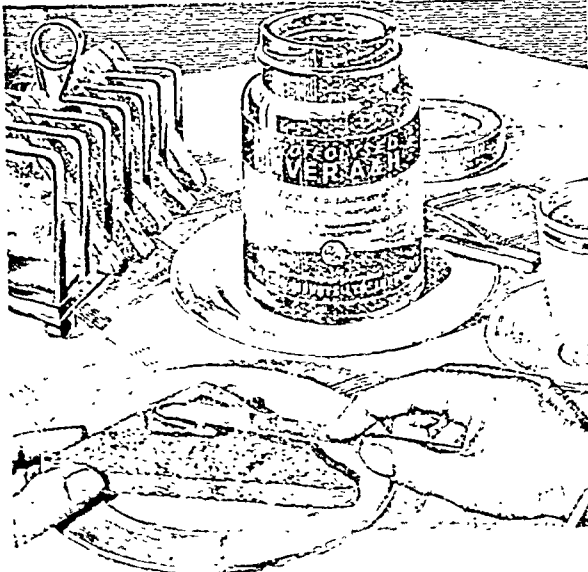
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abscesses under the diaphragm are a source of great anxiety. Does the Fowler position help to do this? The forces governing the movement of fluids within the peritoneal cavity are threefold: gravity, capillary attraction, and differential pressure. Spalding has shown convincingly that gravity is the least important of these, at least when the peritoneal cavity is not exposed to atmospheric pressure. The peritoneal cavity is exposed to atmospheric pressure only for a short while after a drainage tube has been inserted and before adhesions have formed, and for these few hours gravity is an effective force. Capillary attraction plays some part, but by far the greatest part is played by differential pressure, fluid tending to move from areas of high pressure to areas of low pressure. Whenever a patient breathes out, the diaphragm rises and draws up the liver in its wake causing an area of low pressure in the potential space between it and the liver. This region of low pressure attracts fluid to it, and there is on this account a tendency for fluids to collect in the subphrenic space whatever position is assumed in bed. If, however, the patient is propped up, the weight of the liver increases the negative pressure in the subphrenic space and increases the positive pressure elsewhere, so that this tendency for fluid to be sucked into the subphrenic space is considerably enhanced, and we are forced to the conclusion that the Fowler position does not in fact tend to localize intraperitoneal collections in the lower part of the peritoneal cavity.

In regard to the other advantages claimed for the Fowler position, it must be conceded that the patient with heart failure breathes more easily when propped up so that the bulk of the liver is not lying against the heart, but in other than cardiac patients the respiratory excursion is not much affected by position, and if the patient is allowed to lie down in bed he will turn first on one side and then on the other, and secure far more adequate gravity drainage for the bases of his lungs than if propped upright and maintained in one position. It is in fact the added freedom of movement when lying flat which is the great argument against the Fowler position. Movement is essential to maintain an adequate circulation rate, particularly in the veins of the calf muscles where post-operative thrombosis arises, and this movement is only possible when the patient is accorded what Rawlands used to describe as 'the Freedom of the bed'. Therefore at all stages in convalescence the patient should be allowed to assume in bed that position which he finds most comfortable. When he feels ill and wishes to lie down let him do so, but encourage him to turn over or, if too ill to turn himself, have him turned over in order to help drainage from the lungs and to prevent bed-sores. As he becomes able to feed himself and as he seeks to read and to write, prop him up so that he is able to do so. In this way we are at least serving the patient's needs and not merely obeying 'laws' which may turn out to be delusions within half a century.

The Treatment of Epilepsy

By DAVID KENDALL

(From the *Practitioner*, Vol. 159, August 1947, p. 143)

THE treatment of epilepsy is a two-fold problem: the education of the patient in the nature of his complaint, and the measures to be taken to reduce the number of fits to a minimum.

EDUCATION OF THE PATIENT

It is essential at the outset that the patient be made aware of the nature of his fits; it is upon this that the success of treatment largely depends. It should be emphasized that the sufferer from epilepsy is not in any way debarred from normal society and that no stigma is attached to the term epilepsy.

False hopes of an ultimate cure should not be raised; indeed it is better that the patient should realize that the tendency to have fits may be permanently present and that in consequence certain modifications in his or her way of living are necessary. It should be pointed out that the taking of medicine or tablets is intended to reduce the tendency to have an attack, the treatment having no intrinsic curative properties. The necessity for complete regularity in treatment should be stressed, and the patient should be warned against quack remedies and cures.

In the case of children the parents should be carefully instructed, and every effort should be made to ensure that the child receives normal schooling, with only those restrictions necessary for the child's own safety. It is, of course, desirable to obtain the close co-operation of the school authorities. It is only in those children in whom mental deficiency is evident, or in those whose fits are very numerous and difficult to control, that it may be desirable that the child be sent to a special school for defectives, or other residential institution.

There are certain general principles in the treatment of epilepsy, the careful observance of which by the patient may materially help to reduce the number of attacks. Regular habits are essential, in particular in regard to sleep. Excessive fatigue should be avoided so far as possible. Moderate amounts of alcohol may be taken unless it is found in the individual patient that this increases the likelihood of a seizure. Meals should be regular, but no special diet is indicated. Constipation must be avoided.

The epileptic should not drive a car, ride a bicycle, swim or climb, nor should he be employed on heights, ladders, or near any unguarded machinery. The patient should in fact avoid all situations in which the occurrence of a fit would endanger himself or others. These remarks apply equally to major and to minor epilepsy.

CONTROL OF ATTACKS

Broadly speaking, the same drugs are used in treatment of both major and minor epilepsy. As a general rule the control of major epilepsy is much easier than that of the minor variety, which not infrequently is almost uninfluenced by any form of treatment.

Two groups of drugs are in common use and are of proved value; bromide salts and various barbituric acid derivatives. Other substances, such as belladonna and borax, are often used as adjuvants and are at times of benefit.

Bromides.—It has been the practice in the past to begin treatment with bromides, adding or substituting barbiturates if inadequate control is obtained. The present trend, however, is to proceed to the latter at the outset. Bromide is usually administered as the potassium or the sodium salt; the latter is preferable. A normal adult dose is 7 to 10 grains (0.45 gm. to 0.65 gm.), thrice daily, but this may be increased up to a total of 40 grains (2.6 gm.) in twenty-four hours, if necessary. It is usual to include in the mixture 1 to 2 minims (0.06 to 0.12 c.cm.) of Fowler's solution in each dose, which is said to decrease the tendency towards a bromide eruption. It must be borne in mind that the long-continued use of bromide salts may produce symptoms of bromism: increasing lethargy and drowsiness, loss of appetite, furred tongue, constipation, slurred speech and, finally, delirium and coma. If this complication is suspected all bromides must be withdrawn and sodium chloride administered by mouth, with intravenous saline if necessary. The prolonged use of Fowler's solution may produce evidence of chronic arsenical poisoning, in particular a cutaneous rash and pigmentation, and it is advisable only to include this in the mixture in alternate months.

Of the barbiturates, phenobarbitone (luminal, gardenal) is the most widely used. This is given in doses of 0.5 grain (32 mg.) to 1.5 grains (0.1 gm.) t.d.s., to an adult patient. Children are quite tolerant of phenobarbitone and it is safe to administer it to

infants as young as three months in doses of $\frac{1}{2}$ grain (8 mg.) twice or thrice daily.

Toxic effects of phenobarbitone are uncommon and manifest themselves by drowsiness, a morbilliform or erythematous rash or, more rarely, dizziness and ataxia. These symptoms are usually relieved by a reduction in dosage. Phenobarbitone may be combined with bromide in a mixture if the soluble sodium salt is used. This has the disadvantage of instability, and if it is desired to give both drugs it is better to give them separately.

When the fits are inadequately controlled by phenobarbitone, methalonyl (prominal) may prove effective in doses of 1 to 3 grains (65 mg. to 0.2 gm.), twice or thrice daily.

Recently a new barbiturate, sodium diphenyl hydantoinate (epanutin, dilantin) has been extensively used, both alone and in combination with phenobarbitone. The combination is usually the more effective. Diphenyl hydantoin is given in individual doses of 1.5 grains (0.1 gm.), and it is unwise to give this dose more than four times in twenty-four hours. When used in combination with phenobarbitone a suitable dosage would be diphenyl hydantoin, 1.5 grains (0.1 gm.) t.d.s., with phenobarbitone $\frac{1}{2}$ grain (32 mg.) t.d.s., with correspondingly smaller doses for children. This drug may produce toxic symptoms—diplopia, vertigo, ataxia, nausea and skin rashes; these symptoms usually respond to a reduction in dosage.

All these drugs are equally suitable for both major and minor epilepsy. The latter may benefit from the addition of tincture of belladonna, 5 to 10 minims (0.3 to 0.6 c.cm.) to a bromide mixture.

In recent months a new barbiturate, 3, 5, 5-trimethyl-oxazolidine -2, 4-dione (tridione), has been introduced into this country following successful trials in the United States. This drug, administered in doses of 0.3 gm., three or four times daily, has proved very effective in the treatment of minor epilepsy, and preliminary trials in this country tend to confirm this, but it is too early to draw definite conclusions. Toxic effects include gastro-intestinal irritation and photophobia, which are an indication for reduction in dose or withdrawal of the drug. It should not be administered in the presence of renal or hepatic insufficiency.

In a number of patients the attacks tend to occur at certain definite times. In these cases suitable adjustment of the timing of drugs is indicated. In the case of nocturnal epilepsy a larger dose should be taken at night than in the morning. In some female patients attacks occur only at the time of the menses, and provided that the time of the menses is exactly known it is justifiable to give treatment only for the few days before the fit is to be expected. This, however, places a burden upon the patient's memory and intelligence and is therefore not always applicable.

TREATMENT OF THE ATTACK

The treatment during a fit consists of measures to prevent the patient injuring himself, and steps should always be taken to prevent biting of the tongue by the use of a suitable gag. The wise patient provides himself with a hard rubber gag, and may be able to apply it himself should his fits be preceded by a definite aura.

Mention must be made of the treatment of *status epilepticus*, since it is not commonly realized that this is a very dangerous condition, having a mortality of 20 to 30 per cent. The patient must be put to bed in a quiet darkened room with the minimum of handling, and should be brought as quickly as possible under the influence of barbituric drugs. An effective method is to administer slowly 0.5 gm. (7.5 grains) of sodium amytal intravenously, and follow this immediately with an intramuscular injection of an oily phenobarbitone solution, 3 grains (0.2 gm.), the latter to be repeated in four hours. An enema should be given, and further sedation if required can be obtained by the use of paraldehyde, 240 to 480 minims (14 to 28 c.cm.), per

rectum. Inhalation of anaesthetics and the administration of morphine are not advisable. Usually the fits will cease rapidly with this regime, and when the patient becomes conscious large doses of phenobarbitone should be continued by mouth, to be reduced to a more normal dose over a period of days.

The above treatment of epilepsy refers only to the idiopathic form, although the same general principles apply to the treatment of fits which are a manifestation of organic disease, and may be used to supplement the treatment of the primary condition present.

Carcinoma of the Large Intestine

By R. J. JACKMAN *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 134, 16th August, 1947, p. 1287)

In the group studied, more than half (54.3 per cent) of all patients with carcinoma in any part of the large intestine had lesions which could be palpated by digital examination of the rectum. About a fourth (23 per cent) of the patients in this group had received some form of treatment for disease of the colon or rectum, but not for carcinoma, during the course of their symptoms arising from the unsuspected carcinoma that was within the reach of the examining finger.

An additional 16.2 per cent of all the patients who had carcinomas anywhere in the large intestine had lesions which were within the reach of the sigmoidoscope. A fourth (25.8 per cent) of this group had received treatment for some disease other than the carcinoma, which had remained undiscovered.

Patients who had carcinomas of the large intestine that were beyond the reach of the examining finger and sigmoidoscope constituted the remaining 29.5 per cent of the total series of 817. Of this group, 28.4 per cent had carcinomas that were diagnosed by roentgenologic studies of the colon, and 1.1 per cent had lesions that were discovered at abdominal surgical exploration. In this group, during the period of symptoms from carcinoma, only 9.9 per cent of the patients had received treatment directed toward any other condition.

Pyrexia with Hypernephroma

By C. H. CATLIN *et al.*

(Abstracted from the *Lancet*, ii, 2nd August, 1947, p. 170)

Two cases of pyrexia of uncertain origin, eventually shown to be due to hypernephroma, are described. The pyrexia was attributed to a central necrosis in the tumour in one of them, and to secondary deposits in the other.

In pyrexia of uncertain origin hypernephroma should be considered a possible cause.

Pseudomonas pyocyanea Meningitis following Spinal Analgesia

By I. M. DAVIDSON

(Abstracted from the *Lancet*, ii, 1st November, 1947, p. 653)

Two cases of *Ps. pyocyanea* meningitis following spinal analgesia are described. One patient recovered after treatment with sulphamerazine; the other died.

The source of the infection could not be traced; but in a similar case (not described here) the source was so-called sterile water in the operating-theatre.

Emphasis is laid on the importance of a rigid technique of asepsis in lumbar puncture, whether for diagnostic or anaesthetic purposes.

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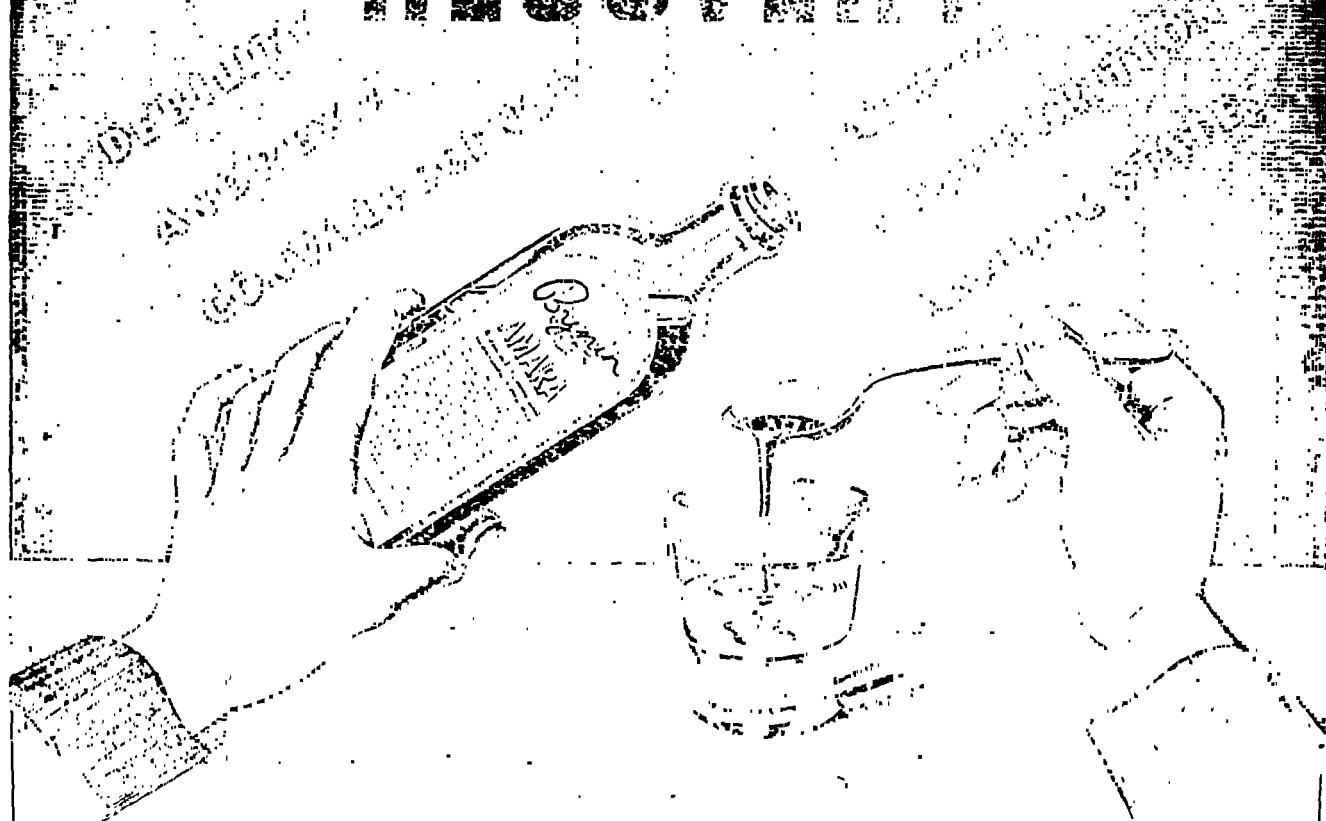
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Quinone and Hydroquinone as Industrial Hazards

(Abstracted from the *British Medical Journal*, ii, 22nd November, 1947, p. 828)

HYDROQUINONE is well known to amateur photographers as a developer. An ophthalmologist practising in Kingsport, Tennessee, where the Eastman Corporation have a factory which makes developers and other photographic products, saw a number of workmen who had brown stains on their conjunctivæ. Investigation soon showed that there were as many as 50 cases of conjunctival staining or corneal opacity among men who had been in contact with either quinone vapour or hydroquinone dust. This sequence of events, which is classical in industrial toxicology, is described in two recent papers on the noxious actions of quinone and hydroquinone.

The ocular signs of the condition were in the interpalpebral fissure. The conjunctiva showed minute spherical deposits of brown or black pigment and the cornea a superficial green-brown stain and—of more serious significance—greyish white opacities at varying depths. Biopsy of the conjunctiva from one case revealed the deposition of large brown globules in the basilar cells near the basement membrane, and of a more finely divided and more widely distributed intercellular pigment. After removal from exposure the pigmentation gradually disappeared, but the corneal opacities remained; apart from the ocular condition no hæmatological or other systemic effects could be detected. The degree of eye injury was correlated with the length of time the workmen had been employed in the dangerous environment, though there were marked differences in individual susceptibility. Staining of equivalent severity developed in one man in one year and in another in over 13 years.

Folic Acid Therapy in Non-tropical Sprue: Results of Treatment in Seven Cases

By J. F. WEIR
and
M. W. COMFORT

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. 32, October 1947, p. 1231)

THE following statements seem justified from our observation of this group of seven cases of non-tropical sprue. Treatment with folic acid has not resulted in improvement in the sense of well-being or in gain in weight or strength that could not be accounted for by increased intake of food and natural remission of the disease. The frequency or severity of the exacerbations of the intestinal manifestations of the disease has not changed. The hæmatologic response has been disappointing since anæmia and macrocytosis have persisted. All this is in contrast to the favourable results reported in the literature regarding response of tropical sprue to treatment with folic acid. Whether the two conditions are different or whether the condition in our cases had advanced to an irreversible stage and become resistant to treatment with folic acid is impossible to state. These results indicate that, in some cases at least, non-tropical sprue does not respond favourably to treatment with folic acid.

The Present Status of Tonsillectomy

By W. A. MILL

(Abstracted from the *Practitioner*, Vol. 159, December 1947, p. 427)

Most authorities agree that tonsillectomy should not be done in the very young child.

Careful diagnosis.—In deciding whether or not the operative removal of the tonsils and adenoids should be carried out, not only must a clinical assessment of the local condition be made but due weight must be

given to the history and to the findings of a general examination. Careful questioning will reveal many 'colds' to the attacks of allergic rhinorrhœa; the pale 'allergic' nasal mucosa will often be recognized, and in such cases, which do not benefit by the operation (unless there are other indications), a family history of allergic troubles will often be found. Sinusitis is common in children: a large mass of adenoids may be present and may require removal in these cases, but it is important to avoid operations on patients in whom the sinusitis is unrecognized, as little benefit will, as a rule, result. It is now much more easy with modern x-ray methods to make the diagnosis of sinusitis than was formerly the case.

History and examination.—The taking of a careful history will disclose the number and nature of the attacks of sore throat and their severity; whether there is at any time enlargement or tenderness of the cervical lymphatic glands; whether a foul taste is sometimes noticed in the mouth or a foul smell in the nose.

In examining the patient the teeth and mouth as well as the tonsils must be examined and the examination should always include inspection of the nose and nasopharynx and transillumination of the sinuses. It is hard to define the appearance of the septic tonsil. Size will be noted but this alone is not a dependable criterion. Persistent redness of the tonsil and the adjacent mucosa suggests underlying infection. Pressure with the spatula will empty the crypts; white, cheesy epithelial debris is not regarded as abnormal, but tonsils containing purulent matter or material with a foul taste and smell should be suspect. The guilty tonsil is often small, buried and fibrotic. Soft-looking tonsils are often the cause of symptoms. Tonsils giving rise to exacerbations of acute inflammation, often with cervical gland enlargement, should be condemned. There may be systemic signs of sepsis, such as leucocytosis, low-grade pyrexia and an increased blood sedimentation rate. The patient must be questioned to see if any relationship between tonsillar inflammation and the onset or exacerbation of any systemic disorder can be established.

INDICATIONS FOR OPERATION IN CHILDREN

Recurrent tonsillitis.—The principal indication for operation both in children and in grown-ups remains recurrent attacks of tonsillitis.

Impaired nasal respiration.—Interference with normal nasal respiration by day or by night is rightly regarded as an indication for operation. Certain alterations of the voice, the dead 'nasal' voice of adenoids and the thick muffled voice of enlarged tonsils and adenoids, are cured by operation and correct after-treatment which may involve, of course, subsequent speech training.

There is much less tendency in these times to remove the tonsils just because it has been decided that the adenoids should be operated on; only if the tonsils demand removal is this done, and here again it must be emphasized that parental pressure must sometimes be resisted.

Colds.—Children are often referred for operation because they suffer from frequent colds, particularly winter colds. The results of operation have often been disappointing. Kaiser suggests that operation is advisable only in those cases in which it can be shown that the tonsils and adenoids are obstructing the air passages or harbour infection, in such cases beneficial results may be anticipated.

Enlarged cervical glands.—Chronic cervical lymphadenitis is a certain indication for operation.

Ear trouble.—Attacks of deafness due to Eustachian catarrh; recurrent attacks of earache and otitis media, and chronic otorrhœa often indicate that operation should be performed. The removal of adenoids will sometimes be sufficient; care will of course be taken to exclude sinusitis as a cause of the symptoms. Nowadays the removal of tonsils and adenoids in cases of chronic otorrhœa is probably much less often carried out as a routine measure than formerly; so often has it been found that the cause of the continued otorrhœa, is infection of the mastoid antrum and cells. This

diagnosis is suggested by continued, and often copious, otorrhoea and pronounced deafness; considerable help in diagnosis is given by careful x-ray examination of the mastoid.

The Treatment of Ulcerative Colitis

By W. I. CARD

(Abstracted from the *Practitioner*, Vol. 159, December 1947, p. 490)

THERE is still no satisfactory treatment of ulcerative colitis. A course of penicillin and sulphaguanidine, by destroying some of the secondary bacterial invasion of the ulcers, may do good but this treatment is in no sense specific. Morton Gill has suggested the use of an extract from hog's intestinal mucosa but this does not constantly provoke a remission and has proved disappointing. Thiouracil has recently been suggested. Myxoedematous patients are, of course, often constipated and, by producing a degree of hypothyroidism, thiouracil may inhibit intestinal activity and reduce the diarrhoea. I have only seen it do good when it was pushed to this extent and a definite goitre resulted. This does not seem a very practicable form of treatment but is warranted if there is any suggestion of hyperthyroidism; it must, however, be given with the usual precautions. The anaemia in ulcerative colitis is due to loss of blood, secondary malnutrition and infection. It can usually be treated successfully with transfusion of packed cells in the first instance, and maintenance of a normal or nearly normal blood level with as nutritious a diet as possible, containing animal protein, adequate vitamins, and small doses of iron. Iron is usually tolerated as ferrous sulphate if it is given in very small doses after meals and slowly worked up to the usual dose of 3 to 5 grains (0.2 to 0.32 gm.). If there is lenteric diarrhoea, dilute hydrochloric acid 30 to 60 minims (1.8 to 3.6 c.cm.) in water with meals, may stop it. Treatment of the anaemia is an essential part of therapy as healing of the ulcers can hardly be expected to occur in its presence.

Flavouring Paraldehyde

(From the *Practitioner*, Vol. 159, December 1947, p. 494)

ACCORDING to *The Journal of the American Pharmaceutical Association* (July 1947, 8, 366) the Florida Bureau of Professional Relations, conducted from the University of Florida School of Pharmacy, is recommending the following formula for an emulsion of paraldehyde:—

Tragacanth	0.5 gm.
Paraldehyde	45.0 gm.
Distilled water	20.0 c.cm.
Fluid extract of liquorice	8.0 c.cm.
Syrup	to 120.0 c.cm.

Each teaspoonful contains about 2 c.cm. of paraldehyde. To improve the flavour it is recommended that each dose should be administered well diluted with iced water or chilled fruit juice. It is also said that preliminary cooling of the mouth by a cold drink is helpful in disguising the characteristically unpleasant flavour of the paraldehyde.

Reviews

PHARMACOLOGY AND THERAPEUTICS (OFFICIAL AND NON-OFFICIAL) WITH SPECIAL REFERENCES TO TROPICAL DISEASES. B.P. 1948.
By M. A. Kamath, M.B. & C.M. Published at Planters Lane, Mangalore. Pp. 441, with three appendices. Price, Rs. 7-8

THE book was published by Dr. Kamath originally in 1933. The present volume embodies all the original

information in addition to the incorporation of several official and non-official remedies and several B.P. Addenda which brings it in line with the B.P. 1948.

This book is divided into three parts and is further divided into 14 chapters, dealing with pharmacology and therapeutics of various official and non-official drugs in the pharmacopoeia, diagnostic agents as fluoresceine, iodophthalein, thorostat, diadone, etc., short notes on important coal-tar derivatives as gonacrin, rivanol, brilliant green, chinisol, etc. The book also includes a brief concise description of modern war-time discoveries as D.D.T. and its application as an insecticide; paludrine, its use in malaria and other protozoal infections and antibiotics as penicillin and streptomycin.

The book also deals with a few indigenous drugs of India of fair repute and those which can be easily substituted for the present B.P., organic and vegetable drugs.

This book is considered as a text and handy volume for medical students and the practitioners in the country practice, who will be able to find all the necessary information they may require without searching for extensive treatises on the subject.

It would have added to the value of the book if the author had added another appendix dealing with International Standards for the biological drugs, posological tables, the pharmacology and uses of snake venoms and treatment of snake-bite poisoning.

The author is however congratulated for his success in incorporating so much information in 440 pages. The appendix on Madras Hospital Pharmacopoeia will be very useful to the students and practitioners of Madras province in particular.

J. S. C.

RECENT ADVANCES IN OBSTETRICS AND GYNÆCOLOGY.—By Aleck W. Bourne and Leslie H. Williams. Seventh Edition. 1948. J. and A. Churchill Ltd., London. Pp. viii plus 326 with 85 illustrations. Price, 21s.

THE seventh edition of this intrinsically valuable book will be received gratefully by persons for whom it is meant, viz, the students of advanced obstetrics and gynaecology and practitioners of this speciality.

Six entirely new chapters have been introduced. Some others have been suppressed. The first two chapters call for special praise and appreciation—by practitioners in the East with whom 'Nutrition during gestation period' and 'Treatment of oedematous conditions' during the same period are everyday problems in these post-war days. The complex subject has been dealt with in a very easy and pleasant style.

The wealth of physiological and anatomical details in the chapter on Lactation is another special feature. The authors say, in the preface, 'we have been impelled to devote some space to purely physiological details'. The reviewer and readers of this stamp would benefit for such and similar other 'impellations' on the authors' part.

In the Section on Gynaecology—the chapter on Stress Incontinence has been specially well written. The diagrams are of great practical value to the operating surgeon. Who will not admire the frank honesty of the authors—when they say 'We can speak feelingly for though we have had some very successful cases, we have also had one which presented almost every possible mishap' (pp. 267)? Then follows the elaborate and straightforward description of a series of 'mishaps' indeed. It is only a past master in the job who can so clearly describe his difficulties and be a source of encouragement and cheer to the junior colleagues following the footsteps of the master.

It is impossible to keep oneself away from unqualified praise for this valuable work—not only in the 'zaivette' of the text but also in its get-up, printing and illustrations—these latter have always been a speciality with the publishers Messrs. J. and A. Churchill Ltd

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THE DIABETIC A.B.C.: A PRACTICAL BOOK FOR PATIENTS AND NURSES.—By R. D. Lawrence, M.A., M.D., F.R.C.P. (Lond.). Tenth Edition. Published by H. K. Lewis and Co., Ltd., London. Pp. 90, size Demy 8vo. Price, 4s. net

IN the recent edition of Dr. Lawrence's *Diabetic A.B.C.*, no fundamental changes have been made except that in view of the post-war diet situation, a few fresh recipes have been added to vary the general monotony of the diabetic diets.

We trust this book would be as popular among diabetic patients as its predecessors.

J. P. B.

VITAL STATISTICS AND PUBLIC HEALTH WORK IN THE TROPICS INCLUDING SUPPLEMENT ON THE GENEALOGY OF VITAL STATISTICS.—By P. Granville Edge, O.B.E., D.Sc. Ballillère, Tindall and Cox, London. 1947

THE author notes the importance of vital statistics and considers some of the difficulties encountered in their collection in the tropics. Fears and superstitions associated with this type of work are described. The author then describes methods of estimating the size of a population when the census method is not used. This is not a book explaining the theory and mechanism of statistics but more of an essay on the difficulties encountered by statisticians in the field in tropical countries. The last seventy-five pages are an essay on the genealogy of vital statistics.

E. J. S.

A PRACTICAL HANDBOOK OF HOSPITAL ADMINISTRATION.—By Sardar Sahib Dr. Rajinder S. Grewal, M.B.E., F.R.F.P.S. (Glas.), L.M.S. (S'pore), M.A., LL.M. (U.S.A.), Barrister-at-Law, Civil Surgeon, Mandalay-Burma. Printed by Caledonian Printing Company, Limited, 3, Wellesley Place, Calcutta. Pp. 149

THE author has touched on the various problems from the site selection for a hospital building to all the details and problems that may arise and a medical officer may have to face in the day-to-day administration of a hospital.

Even the forms of letters for correspondence have been shown.

The author has very exhaustively dealt with details like hospital buildings, making of indents to equip the hospital initially and also subsequently—very useful instructions will be found here, even supplementary indents will not be missed.

Facsimiles of forms and books have also been shown. Fire-fighting scheme has not been forgotten.

This book was written with a view to acquainting the Superintendents, Medical Officers and House Surgeons with the various aspects of the administration of Famine Relief Hospitals, but I am quite sure that this book will come out as a great help to those who are responsible for the running of a permanent hospital, and with this idea every one responsible for the administration of these hospitals should possess a copy. I fully agree with the remarks made by Col. Treston, Ex-Inspector-General of Civil Hospitals, Burma, made in the short foreword introducing the book. This book appears to be the first of its kind and should be useful.

A. S.

AN INDEX OF TREATMENT.—By Sir Robert Hutchison. Publishers: John Wright & Sons Ltd., 42/44, Traingle West, Bristol 8. Pp. 984. Price, 84s.

MORE and more height is added to this pillar of British medical wisdom with each new edition. Like its predecessors the present, 13th, edition is a complete guide to treatment except in management of labour.

The editor and his assistant have collaborated with 72 contributors to revise the book thoroughly, with a

view to including recent advances in therapeutics and associated advances in aetiology of diseases, etc. Over 80 articles are new or have been re-written.

The items run in alphabetic order. A supplementary index affords further aid in finding the measures required.

As an example of the associated advances in aetiology may be mentioned the observation (under sterility in the male, p. 792) that repeated miscarriage may result from faulty sperm.

Minor faults are: (1) Omission of the bacillary form of rat-bite fever. (2) The dose of the toxin in the Schick test. It should be 0.2 cc., not 2 cc. (3) The minim equivalent of mil. In the conversion table 1 mil. is given as '= $\frac{1}{15}$ (nearly 17) minims', 16 would be more appropriate.

The aesthetic effect is worth recording in these days of scarcity, strict utility and austerity. The well printed and equally well-illustrated volume bound in rexine is an asset to one's desk. The price is reasonable.

S. D. S. G.

BOOKS RECEIVED

1. *Annales Medicinæ Internæ Fennicæ*. Vol. 35, 1946, Fasc. 2.
2. *Chikitsa-Jagat*. Vol. XX, No. 2, Dec. 1948.
3. *Howrah Municipal Gazette*.
4. *Proceedings of the Alumni Association of the King Edward VII College of Medicine, Singapore*. Vol. 1, No. 1, October 1948.
5. *Enquiry*. Vol. 1, No. 3.
6. *Journal of Ayurvedia*. Vol. 1, No. 1, January 1949.
7. *Indian Research Fund Association, Special Report, No. 17. Summary of the findings of investigation into the causes of maternal mortality in India*. By Dr. S. Pandit, w.m.s. June-1948.
8. *Compost Bulletin*. Vol. 1, No. 3, September 1948.
9. *Why India Starves and the Remedy*. Shrimati Mira Behn. (With a Hindi supplement.)
10. *Transactions of the National Institute of Sciences of India*. Vol. III, No. 1, pp. 1-166 (15 charts). On nuclear energetics and B-activity. Part II, By A. K. Saha, S. Ghoshal and S. Das.

Correspondence

GLUCOSE INJECTION

[In connection with the letter on the above subject published in the *I.M.G.*, October 1948, p. 484, Messrs. W. T. Surén & Co., Ltd., Bombay, have sent a reply to the correspondent referring him to an article on 'Reactions to Intravenous Solutions', by Lee Rademaker, M.D., *J.A.M.A.*, 27th December, 1947, p. 1140, and to another article on 'An estimation of the sources and the quantitative methods of testing pyrogen' by Wylie et al., *Quart. Jour. of Pharmacy and Exptl. Pharmacol.*, July-September 1948, p. 240. They also supplied an abstract of these two articles which is reproduced below.]

'Reactions do occur with a frequency inexcusable in the light of the present-day knowledge. Commercial houses have, in general, attempted to correct the situation. But, too often contact is made only with a purchasing agent who looks at the increased cost of the material presented and refuses to buy it until forced by the medical staff's complaints about reactions.'

Seibert (1923) demonstrated that the substance responsible was the product of bacteria which exists in the river water and in tap water. Distilled water, if

used before bacterial contamination had time to become effective, does not cause any reaction. Pyrogen is a filtrable toxic product of bacterial growth not found in an appreciable quantity in bacterial bodies. They are not decomposed by the amount of heat generally used to sterilize solutions. They pass through ordinary distilling apparatus, but could be separated by spray-trapping devices and also by multiple baffle plates and deconcentrator tubes.

'The care of the glassware and tubing remains the predominating factor in production of reactions.' The type of rubber and corks, specific in concentration temperature and speed of injection have nothing to do with the problem. *'The main fact is that tap-water is the source of contamination and any glassware or tubing rinsed or washed in tap-water will produce pyrogen unless sterilized within an hour.'*

In commercial houses steam jets simultaneously wash and sterilize glassware, whereas in hospitals a simple rinsing is often considered sufficient to cleanse containers before they are filled, to be sterilized when it is convenient. Contamination follows and pyrogen is produced before the solution is sterilized. Tubing rinsed with tap-water and exposed to air for only an hour will be contaminated, and even the film of moisture inside an intravenous needle may contain enough pyrogen to cause the reaction.

Instances in which reaction has not occurred following intravenous infusion with equipment that has been washed but not immediately sterilized may be attributed to the fact that water from some taps may contain pyrogen producing bacteria in a lower concentration than that found in other taps. The concentration is greater in water which has been stagnant in pipes for some time.

It should be remembered that pyrogen is readily soluble; distilled water easily removes it from tubing and glassware, but it is imperative that even this rinsing be followed by *immediate sterilization*. If the presence of pyrogen is suspected in tubing or needles that are set up for use, reactions can be prevented because of the extreme solubility of the pyrogenic substance, by rinsing and wasting about 100 cc. of the pyrogen-free solution before the needle is inserted in the vein.

Pyrogen can accumulate in the distilling apparatus maintained by many hospitals for use in preparing their solutions. This is not to be underestimated as a source of trouble, but reactions can be averted by periodic cleansing (Lee Rademaker, M.D., J.A.M.A., 27th December, 1947, p. 1140).

Recently, this subject has been worked out in detail by Wylie and Todd in an article on 'An examination of the sources and the quantitative methods of testing pyrogen' in the *Quarterly Journal of Pharmacy and Pharmacology*, July-September 1948, p. 240.

All bacteria tested showed production of pyrogen; Gram-negative bacilli showed much greater powers of pyrogen production than Gram-positive types, while yeast and moulds showed no detectable quantities of pyrogen. Neither storage nor normal process of sterilization by autoclaving at 115°C. for thirty minutes had the effect of removing pyrogen. Two types of fevers were observed, one showing single peak followed by a fall to normal body temperature and the other a double peak, the second peak of which seemed to depend on the presence of the bacterial cells because their removal largely eliminated it. These experiments with pure cultures of various types of bacteria, yeast and moulds were carried out on rabbits by intravenous solutions and by accurate measurements of temperature.

The above facts show that though the manufacturing firms usually take meticulous care in their preparations in order to prevent contamination with pyrogenic substances and each lot is biologically tested as a further precaution yet, it is extremely easy to get contamination by pyrogen even with a slight lack of care in observing minutely all the rituals—scientific department, W. T. Surén & Co., Ltd., Bombay.

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL JASWANT SINGH, Director, Malaria Institute of India, is temporarily appointed as *ex-officio* Additional Deputy Director-General of Health Services, with effect from the 8th November, 1948.

The services of Lieutenant-Colonel C. Mani, Additional Deputy Director-General of Health Services, are placed at the disposal of the World Health Organization for appointment as Regional Director with effect from the 15th December, 1948.

The services of Dr. F. E. Buckler are placed at the disposal of the Military Secretary to His Excellency the Governor-General with effect from the 1st April, 1948.

Dr. T. B. Medappa is confirmed in the post of Civil Surgeon, Coorg, with effect from the 12th July, 1948.

LEAVE

Major R. D. MacRae, an Agency Surgeon, Legation Surgeon, Kabul, was granted leave on average pay for 8 months, and on half-average pay for 1 year 2 months and 26 days, with effect from the afternoon of the 14th January, 1948, preparatory to retirement.

RELINQUISHMENT

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Lieutenant-Colonel.

LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Major Emrys Lloyd Jones. Dated 1st April, 1948.

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Original Articles

CLINICAL FEATURES AND LABORATORY DIAGNOSIS OF XK OR MITE-BORNE TYPHUS AS OBSERVED IN 102 CASES IN THE BARRACKPORE AREA

By K. V. KRISHNAN

R. O. A. SMITH

P. N. BOSE

K. N. NEOGY

B. K. GHOSH ROY

and

M. GHOSH

(From the Bengal Typhus Enquiry at the All-India Institute of Hygiene and Public Health, Calcutta, partly financed by the I. R. F. A.)

WITHIN the last ten years several reports of the occurrence of typhus fevers of all three serological varieties have been published from almost all the provinces of India. XK typhus (mite-borne) appears to be common in most places, X19 typhus (murine, flea-borne) coming second, X2 typhus (the true nature of which is not yet clearly understood) coming third and X19 typhus (louse-borne) coming last. Although the total mortality caused by typhus fevers is not very high the morbidity caused by them is increasing rapidly. While a few years ago these fevers were not considered to be of much public health importance in India, to-day they are undoubtedly as important as the enteric group of fevers in the areas where they occur.

Between 1946 and 1948, 102 cases were diagnosed as typhus in Barrackpore by the Enquiry into Typhus in Bengal at the All-India Institute of Hygiene and Public Health, Calcutta. This number represents merely a fraction of the total number of cases occurring in this area. 72 per cent of these cases were XK typhus, 19 per cent X19 (murine) and 9 per cent X2. In 64 cases of this series the diagnosis was based on (i) clinical findings, (ii) Weil-Felix reaction, (iii) isolation of rickettsia by animal inoculation, and (iv) study of pathological lesions caused in experimental animals such as guinea-pigs and mice. In the other 38 the diagnosis was based on clinical findings and a suggestive Weil-Felix reaction; no animal inoculations were done in this group for confirming diagnosis. The clinical and laboratory data collected with respect to all these cases have been analysed and the results are presented in this article. Although accounts of the clinical features of typhus cases are found in many publications the relative importance of serological tests and animal inoculation in the diagnosis of typhus fevers has

not been sufficiently stressed. Furthermore, the average practitioner is not yet fully aware that typhus cases are occurring in large numbers among the civilian population in endemic areas and that many of these cases are still being erroneously diagnosed as para-typhoid, dengue, influenza or classified as P.U.O.s, because reliance is placed on clinical findings and laboratory aid is seldom resorted to. Since a sure diagnosis of typhus can only be made in the laboratory and too much reliance cannot be placed on the variable clinical findings (except in the severe forms) it is hoped that this article on the clinical and laboratory diagnosis of typhus fevers in general and of XK typhus in particular will be of interest.

Clinical diagnosis

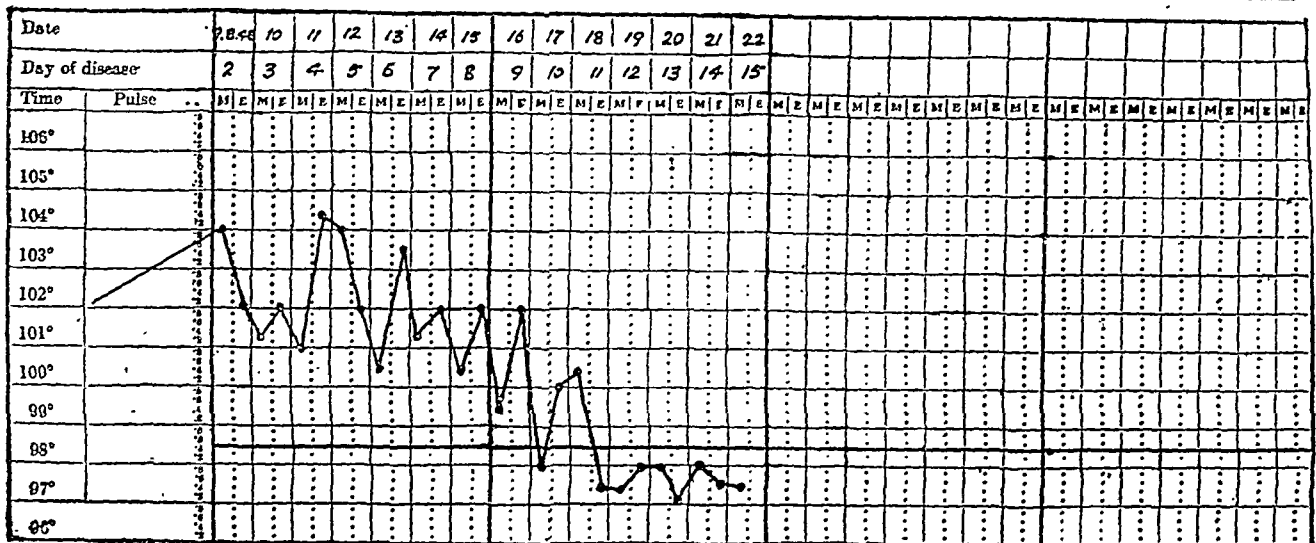
It is generally recognized that the clinical features of typhus cases are apt to show marked variations. The variations may be ascribed to differences in the causal agent, mode of transmission and immunity status of the population affected. From a study of the clinical features of cases in the Calcutta-Barrackpore area it is found that typhus cases can be divided clinically into two types 'mild' and 'severe'. In this area 80 per cent of cases belong to the mild and 20 per cent to the severe type. Due to the infrequent occurrence of several of the characteristic symptoms in the majority of mild cases, it was found impossible to diagnose them on clinical evidence alone. Laboratory aid had to be sought to obtain a diagnosis in these cases. In the severe cases and in a small percentage of mild cases (i.e. in all about 40 per cent of cases) the symptoms were generally characteristic and a provisional diagnosis of typhus could be made. But laboratory aid had to be sought for determining the type of typhus. Clinically, it was not possible to distinguish between the three types of typhus (XK, X19 murine and X2). The differences in the clinical features were not clear cut. In a few of the cases in which some characteristic symptom or other such as eschar or petechial rash was present, one could hazard a guess as to the type but this needed to be confirmed by laboratory tests.

The clinical features of XK typhus which is the predominating type in the Barrackpore area are presented below :

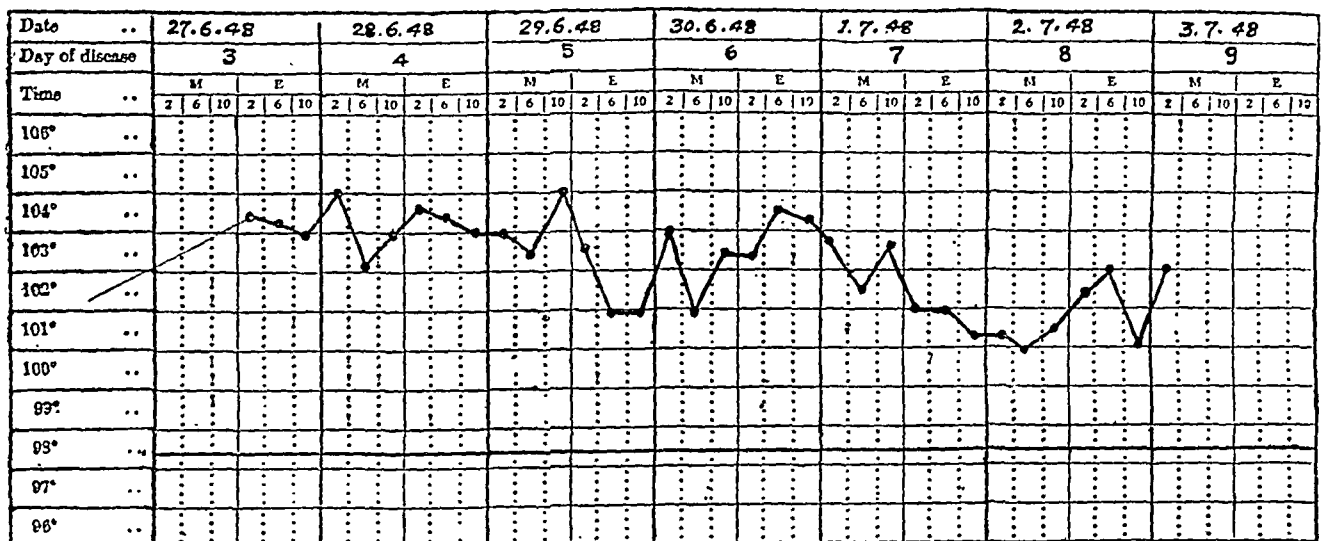
The onset of fever in the majority of cases was sudden. In mild cases the temperature went up to 101°F. and 102°F. and occasionally to 103°F. In the severe cases it rose higher and in some reached 105°F. In 60 per cent of the cases fever was remittent in type and in 40 per cent it was continuous. The total duration of fever varied. In the mild type it lasted about 10 to 14 days with an average of 12 days, whereas in the severe type it ranged from 14 to 22 days with an average of 18 days. The termination was either by crisis or by lysis; both were equally frequent (*vide charts*).

CHARTS.

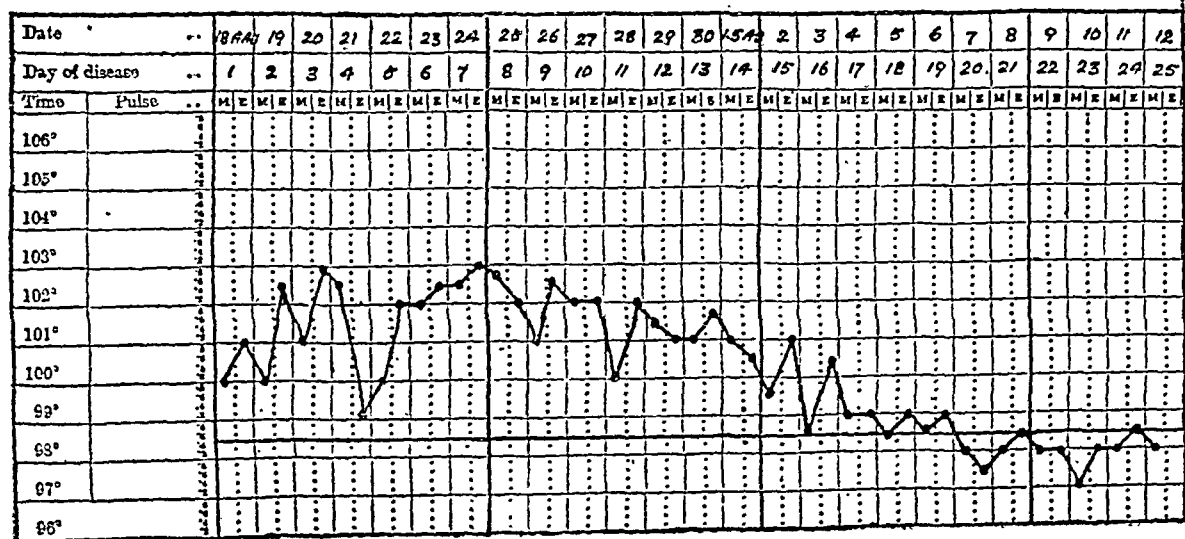
Name Gorakh-nath Age 35 Disease TYPHUS Date of admission 9.8.48 Date of discharge 22.8.48



Name Bhagawandin Age 45 Disease TYPHUS Date of admission 27.6.48 Date of discharge on 3.7.48 Expired at 3.20 A.M.



Name Dr. Smith Age 56 Disease TYPHUS Date of admission 21.4.48 Date of discharge 12.5.48



Headache was complained of by all patients. In the mild type it was present at the commencement of illness and disappeared a few days afterwards. In the severe type it persisted for a much longer period and was complained of even in the second week of illness. In 30 per cent of all cases it was very severe, persistent and annoying. This feature is of diagnostic significance.

Mental dullness was present in all severe cases and in about 40 per cent of mild ones. It was most marked about the end of the first week of illness and persisted for some days. Patients had a vague and sleepy look and there was much delay in comprehending questions and in replying to them. This was very characteristic.

Delirium of a low muttering type was present in 21 per cent of the severe type only.

Sleeplessness was a characteristic feature of most cases. 41 per cent of the mild type and all cases belonging to the severe type complained of this. It was persistent and troublesome in the severe cases and almost the first thing the patient requested the doctor was for 'some medicine to sleep'.

Deafness was another feature frequently observed. It was noticed in 57 per cent of severe cases and in 18 per cent of mild cases. It was most marked during the second week of illness and cleared up quickly after the temperature dropped to normal.

Congestion of the eyes was an early and constant symptom. In the mild cases it lasted for a few days and in the severe cases it persisted till the middle of the second week. This is a valuable diagnostic sign. In about 50 per cent of the severe cases ptosis of the lids was noticed imparting the sleepy look.

Giddiness was complained of by many patients. In 90 per cent of severe cases and in 15 per cent of mild cases it was marked and troublesome.

Lymphadenitis was noticed in 65 per cent of the cases. It was more frequently seen in the severe cases and less frequently in mild ones. The glands of the neck were most often involved; next in frequency were the axillary glands and lastly the inguinal glands. The glands were shotty and tender. Tenderness was very marked in some cases.

Splenic enlargement was noticed in 26 per cent of cases. The spleen was just palpable in most of these. In two, the enlargement was 2 fingers below the costal margin.

Rash was noted in 75 per cent of severe cases and 7 per cent of mild ones. It appeared on or about the 6th day of illness, was macular in type and distributed mainly on the forehead, arms and legs. It invariably disappeared within a day or two of its appearance. The percentages mentioned would appear very low but in view of the fact that rashes are not easily detected in dark-skinned persons and also that many cases were seen by us late in the course of illness, the figures do not represent a correct

estimate of the incidence of rash. Our belief is that if cases are seen early and one is on the look out for rash it will be found in the majority of cases.

Eschar was seen in 5 of the severe cases. None of the mild cases showed an eschar. In two it was a raised papule about the size of a split pea with a red areola round it and in the other three it was a black necrotic ulcer of the same size with a red areola about one inch in diameter. Lymphangitis was present and the glands draining the area were enlarged and tender. The situation of the eschar in 3 cases was the shoulder girdle (in two it was in front and in one at the back); in the fourth case it was on the genitals; and in the fifth on the finger.

Constipation was complained of by the majority of cases and diarrhoea occurred in 6 per cent of cases.

Tongue was found coated and dry in most of the severe cases. In the mild cases it was normal. The coating of the tongue seen in the severe cases of typhus was quite unlike that seen in typhoid. This feature at times helps to distinguish typhus from typhoid cases.

Pain in the muscles was invariably complained of by all patients. Groups of muscles in different parts of the body were affected. The joints were not involved. This feature was helpful in differentiating typhus from dengue cases. In all severe cases and in 32 per cent of mild cases muscular pain was intense and prostrating.

Lung symptoms were noticed in 50 per cent of the severe cases. Congestion of lung was noticed in the second week and crepitations could be heard on auscultation. There was some cough. These symptoms cleared quickly after the temperature came down to normal.

Blood pressure was lowered in the severe cases towards the middle of the second week.

Pulse rate was usually slow in comparison to the temperature at the commencement of illness in all cases. In the severe cases towards the end of the second week it was inclined to be feeble and rapid.

Leucocyte count did not show any significant change in the cases studied.

Urine in the majority of severe cases showed traces of albumin. In the mild cases it was normal.

Case fatality in this series was only 3 per cent, i.e. 14 per cent of severe and nil in mild cases. Death occurred in these cases about the middle of the second week.

From the data presented above it will be seen that the majority of mild cases of XK typhus do not show any characteristic symptom by which one could diagnose the disease with certainty on clinical grounds. Most cases complain only of fever, headache and pain in the body. When congestion of the eyes, mental

dullness, sleeplessness and glandular enlargement are present typhus could be suspected. If rash and eschar occur the diagnosis is almost certain. Mild cases have been mistaken for dengue, para-typhoid and influenza. From dengue, typhus cases can be differentiated by the longer duration of fever, absence of saddle-back temperature, absence of joint pains and presence of asthenia disproportionate to the mildness of the symptoms. From influenza, they can be distinguished by the absence of coryza and by the longer duration of fever and characteristic temperature chart. From para-typhoid, it is often difficult to differentiate. Absence of abdominal symptoms such as diarrhoea and tympanites, and presence of congestion of eyes, may help in diagnosis. But the diagnosis must be confirmed in the laboratory.

The clinical features of the severe cases are generally very characteristic and it is easy to diagnose them as typhus on clinical grounds with a fair degree of accuracy. The congestion of the eyes, the dull and sleepy look, the extreme asthenia, the slow pulse, the rash, eschar and glandular enlargement when present are all very typical. When one or two typical cases have been seen, the clinical picture presented by the typhus cases cannot be easily mistaken for any other disease except typhoid. But the presence of the characteristic furred tongue and abdominal symptoms in typhoid and the presence of eschar and glandular enlargement in typhus help in differentiation. As stated above, the type of typhus can only be ascertained by laboratory procedures.

Laboratory diagnosis

In the laboratory, the diagnosis of typhus is established by (i) Weil-Felix reaction using 'O' suspensions of proteus X19, XK and X2, (ii) complement-fixation test using specific rickettsial antigens, and (iii) animal inoculation (using mice and/or guinea-pigs) for demonstrating the presence of rickettsiae, and associated pathological lesions, such as the Neill-Mooser reaction, or ascites or enlarged spleen. In the present investigation, as suitable rickettsial antigens for the complement-fixation test were not available only the Weil-Felix reaction and animal inoculations were conducted. Diagnosis of typhus was made when positive Weil-Felix agglutination in titre at or above the prescribed diagnostic level was obtained and when rickettsia and characteristic lesions could be demonstrated in experimentally inoculated animals.

Weil-Felix reaction

For the Weil-Felix reaction, suspensions of OX19, OXK and OX2 were used in all cases. These suspensions were prepared and standardized in the laboratory according to the method of Bridges (1944) and compared before use with standard suspensions of OX19, OXK and OX2 obtained from the Military Laboratory, Poona.

Of the cases diagnosed as typhus, 72 per cent proved to be XK, 19 per cent to be X19 (murine) and 9 per cent to be X2. No difficulty was experienced in diagnosing X19 typhus by the Weil-Felix test. The majority of these cases gave agglutination in high titres. A titre of 1 in 500 to 1 in 1,250 for OX19 was obtained in 70 per cent and in 30 per cent the titre ranged from 1 in 250 to 1 in 500. In some of these cases male guinea-pigs were inoculated with crushed blood clot or washed blood cells but the typical Neill-Mooser reaction was not elicited.

The Weil-Felix tests performed on cases of XK typhus revealed that agglutination in high titres is not as frequently obtained in XK typhus as in X19 typhus. Whereas in every case of X19 typhus an increase in titre to or above the diagnostic level for OX19 was obtained, in only 65 per cent of XK typhus were definitely positive Weil-Felix reactions for OXK found. Furthermore, in only 10 per cent of these was the OXK titre over 1 in 500 and among these in a very few only was the highest titre of 1 in 1,250 obtained. In 90 per cent of the positive group the OXK titre ranged from 125 to 250. The diagnostic level in most cases was usually reached by about the 10th day of illness; in some it was not reached until after the crisis or during early convalescence.

In 35 per cent of XK typhus proved by animal inoculation the Weil-Felix reaction did not give a significant OXK titre even on repeated examinations. In 20 per cent the highest titre obtained was only 1 in 50, in 5 per cent it was 1 in 25 and in 10 per cent it was negative. In some of these cases the titre after rising to 1 in 25 or 1 in 50 either remained at that level or came down to a lower level instead of increasing. This feature was noticed in cases belonging to the severe as well as the mild types. Had animal inoculation not been resorted to in these cases, a definite diagnosis would not have been possible.

Of the fever cases seen in the course of this investigation, 231 were non-typhus cases which had been diagnosed as enteric, kala-azar, malaria, influenza or pneumonia. Sera from such cases examined by the Weil-Felix reaction showed that in nearly 30 per cent a positive agglutination in low titres ranging from 1 in 25 to 1 in 50 was present; 68 reacted with OXK, 43 with OX2 and 28 with OX19. Since the highest agglutinin titre in non-typhus cases was 1 in 50, the diagnostic titre for XK typhus was fixed at 1 in 125 or over. But since it was found that 35 per cent of confirmed XK typhus cases also gave low titres, doubtful cases were not rejected straightaway as non-typhus (unless an alternative diagnosis had been made and confirmed) but were investigated further by animal inoculation. If the Weil-Felix reaction only is used, 35 per cent of XK typhus cases are likely to be missed. By resorting to animal inoculation in doubtful and sero-negative cases practically every case of XK typhus could be detected.

In this series 7 cases were diagnosed as X2 typhus by the Weil-Felix reaction. The agglutination titre obtained for OX2 in these cases varied from 1 in 125 to 1 in 250. Sera of these cases also agglutinated OXK and OX19 to a lesser degree (1 in 25 or 1 in 50).

Workers in other parts of India have also reported cases of X2 typhus but what form of typhus these X2 cases truly represent is not yet clear. Their diagnosis on serological grounds has generally proved a bit difficult and animal inoculation has not been very helpful. This type needs to be properly investigated and its aetiology and epidemiology correctly determined in India.

Animal inoculation

For demonstrating the presence of rickettsiae in the blood of patients and for determining the type of typhus, animal experimentation is essential. For these purposes, guinea-pigs, white rats, white mice, monkeys and rabbits have been used; but guinea-pigs and white mice have proved most satisfactory. For diagnosis of murine typhus male guinea-pigs are the best and for diagnosis of XK typhus white mice are preferable. For X2 both guinea-pigs and white mice have been tried, while for some X2 strains, guinea-pigs have proved more satisfactory than mice, for others, neither of the animals have proved suitable. By the use of guinea-pigs and mice the following results may be expected in the different forms of typhus fevers :—

positives. In the early part of the investigation blood clot was used but later on it was given up and only washed cells were used. Injections into animals were given intraperitoneally. The dose for mice was, washed blood cells from 1 cc. of blood suspended in saline and for guinea-pigs, washed cells from 5 cc. of blood.

In XK cases animal inoculation was resorted to chiefly for diagnosis of clinically positive and serologically doubtful cases and for clinically doubtful and serologically negative cases. It was found that in 71 per cent of the first and in 10 per cent of the second group rickettsia could be demonstrated in the endothelial cells from peritoneal scrapings after staining with Giemsa stain. When washed blood cells of XK cases were injected into white mice the animals usually became ill between the 6th and 12th days and in a very few instances somewhat later. On sacrificing these animals about the 8th day rickettsiae could be demonstrated in the peritoneal scrapings in all positive cases. Samples of blood collected from patients in the early and late stages of the disease (3rd to the 16th day of their illness) gave positive results. In all positive animals the pathological lesions met with were ascites and splenic enlargement; the former was very characteristic of XK strains and by no other strain studied was it caused. In a few animals the ascitic fluid was found to be sticky, purulent and blood tinged. Animals not sacrificed in time usually died. Death occurred in most animals about the 10th or 12th day after

GUINEA-PIG				WHITE MOUSE				
	Fever	Characteristic reaction	Death	Rickettsia	Illness	Characteristic reaction	Death	Rickettsia
Louse-borne ..	+++	Nodes in brain	— (+ in some cases).	++	—	Nil. Inapparent infection.	—	+
Flca-borne ..	+++	Neill-Mooser scrotal reaction.	—	+++	+	Lung infection on intra-nasal inoculation.	—	++ Tunica
Tick-borne R.M.S.F.	+++	Scrotal swelling necrosis.	+++	+++	—	Inapparent infection. On intra-nasal infection lung involved.	—	++ ++
Other types, X2		Not yet investigated						
Mite-borne ..	+	Ascites	— in a few +	++	+++	Ascites, spleen enlarged.	++	+++

In the course of the present investigation guinea-pigs and white mice (Haffkine strain) were chiefly used. Blood samples of 66 cases were subjected to animal inoculation. The material inoculated was either crushed blood clot in saline or washed blood cells of the patient. Washed blood cells proved definitely superior and yielded a much higher percentage of

inoculation. In some it took place later and in a few no death occurred.

Guinea-pigs inoculated with washed blood cells from XK cases ordinarily showed a rise in temperature about the 10th day which lasted for about 2 days and then subsided. When sacrificed during the febrile period ascites and enlargement of spleen were found. No scrotal

reaction was seen in any of them. Rickettsiae were found in scrapings from the tunica. These strains however could not be maintained by guinea-pig passage; the virulence seemed to die out on or after the 3rd passage in all strains isolated in Bengal so far. On this account mice were preferred and several strains have now been maintained to the 50th passage and above in mice.

In two cases giving highest agglutination with OX2 animal inoculation was done and rickettsia isolated. Both mice and guinea-pigs were used. In the first case the strain behaved in mice and guinea-pigs like an XK strain and caused ascites and enlarged spleen with presence of rickettsia in peritoneal scrapings. This strain was assumed to be one of XK and not of X2 on this account. The other strain behaved in an entirely different manner. On first inoculation into a guinea-pig and a mouse negative results were obtained. But when the spleen and brain emulsion of the mouse was injected intraperitoneally into another mouse, the second mouse showed rickettsiae on the 10th day and inoculation of infective material from the second mouse proved infective to guinea-pigs also. In the guinea-pig in which it is now being maintained it is causing a characteristic infection with fever and enlarged spleen only; the strain causes no ascites or scrotal reaction and the inoculated animals do not die. Scrapings from tunica of infected animals invariably show rickettsia. Mice do not appear to be as good as guinea-pigs for maintaining this strain. This strain may be considered to be an X2 strain of this area. This will need further investigation. Morphologically also this strain of rickettsia showed some differences from the XK strain. While the XK rickettsiae look like minute coccobacilli and are found in plenty, the X2 rickettsiae are diploid in appearance, look relatively larger and occur in fewer numbers. They are also intra-cytoplasmic.

It will be seen from the data presented that pathogenicity tests are valuable adjuncts to clinical and serological diagnosis and should be done as a routine in sero-negative and doubtful cases. The importance of animal inoculation cannot be over-emphasized if a correct diagnosis of all typhus cases is to be made. In India where the medical statistics has still a big heading entitled 'Pyrexias of unknown origin' it is very important to resort to all available laboratory aid in order to reduce the number under this heading.

Complement-fixation test

In 1941, Bengtson, and Bengtson and Topping demonstrated that with an antigen prepared from yolk sac cultures of rickettsia, complement-fixation test could be done on the sera of typhus patients and that the test gives more specific results than the Weil-Felix reaction. In the present investigation, due to the non-availability

of suitable rickettsial antigens, the complement-fixation test could not be done. But since it was found that in the diagnosis of XK and X19 typhus the Weil-Felix reaction and animal experimentation give very satisfactory results, the need for the complement-fixation test was not felt much. But in the diagnosis of X2 cases in which clear-cut results were not obtained either with the Weil-Felix reaction or with animal experimentation, it was felt that complement-fixation test would be more helpful. From the experience of workers in other countries, this view receives much support. However, for the performance of the test, antigen prepared from local strains of rickettsia would be highly desirable. Local rickettsial strains will have to be isolated, grown in yolk sacs of chick-embryo and antigen suspensions prepared from the culture material. Attempts are being made to do this but X2 cases are few in this area and occur generally in the spring. During last spring only 7 cases were seen and from only one case was a strain isolated. No attempt has yet been made to grow this in the yolk sac. Until this is done, no further information on the value of complement fixation in the diagnosis of typhus can be given. The problem is an important one, specially as there are several foci of X2 typhus in India.

Summary and conclusion

From a study of 102 cases of typhus fever occurring in the Barrackpore area among the civilian population the following conclusions have been drawn :—

That 80 per cent of typhus cases in this area belong to the mild and 20 per cent to the severe type. The total case fatality rate is 3 per cent.

That it is not possible to make a diagnosis of typhus on clinical grounds alone except in about 40 per cent of cases and that in the other 60 per cent laboratory aid has to be sought for establishing diagnosis.

That it is not generally possible to differentiate between X19, X2 and XK cases on the basis of the clinical findings due to the similarity of the characteristic symptoms.

That in 65 per cent of XK cases a sure diagnosis of typhus can be made on the basis of the Weil-Felix reaction. In 25 per cent of cases the agglutinin titre is below the diagnostic level and in 10 per cent negative results are obtained even on repeated examinations.

That the doubtful and sero-negative XK cases can be diagnosed readily by demonstrating rickettsiae in stained preparations of peritoneal scrapings obtained from white mice inoculated intraperitoneally with washed blood cells of patients and sacrificed about the 10th day after inoculation. That the pathological features in these animals are also quite characteristic—ascites being invariably present.

That for the diagnosis of X19 cases the Weil-Felix reaction is highly satisfactory.

That for the diagnosis of X2 cases the Weil-Felix reaction is not always dependable, and animal inoculation is not also of much value. It is possible that the complement-fixation test will be found more helpful, but it has not been tried with local strains.

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THE BREEDING AND MAINTENANCE OF *TROMBICULA DELIENSIS* IN THE LABORATORY FOR EXPERIMENTAL PURPOSES

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THE interest in the life history of the mite *Trombicula deliensis* lies in the fact that it is suspected to be one of the vectors of typhus of the XK serological group in India and Malaya. Before the last great war, fevers of the typhus group were known to exist in certain limited areas in India and the Far East, but the distribution of troops over wide areas in the East during the second world war revealed the widespread nature of the endemic foci of typhus of this type. Bengal which was supposed to be free of such a disease was soon shown to possess many endemic foci, some immediately around Calcutta. Investigations in these foci revealed that rats were infected with *Rickettsia orientalis* the causal agent of XK typhus and that they were also heavily parasitized by larvae of *T. deliensis* the suspected vector. This gave us an opportunity to find out if *T. deliensis* was the carrier of *R. orientalis* in this area. In that connection we had to breed *T. deliensis* in the laboratory. Before one can obtain certain evidence of the rôle of this mite transmission, it is necessary to breed the mite in captivity so that laboratory-bred larval mites will be available in sufficient numbers for use in transmission experiments. This had not been done till now.

Nagayo *et al.* (1917) were the first to attempt the breeding of Trombiculids. They claimed to have obtained a few adults by feeding nymphs on melon, potato, etc. Our efforts to breed *T. deliensis* using such material as food proved fruitless. We found that the nymphs which were

easily obtained were able to find some nutriment from silt. Enriching the silt with bacteria and protozoa did not secure the desired result. At this stage our attention was directed to an article by Wharton and Carver (1946) in which they described the development of a species of *Neoschongastia* by feeding the nymphs on the eggs of insects. Mosquito and sandfly eggs were used by us to feed the last few nymphs remaining at the close of the 1947 season, and it was soon apparent that this food was suitable for nymphs and adults of *T. deliensis* as well.

T. deliensis is most prevalent around Calcutta, just after the first rains in June. It can be found in adequate numbers on the ears of rats up to November after which the numbers diminish very rapidly. As soon as sufficient numbers of *T. deliensis* larvae were obtained, the breeding of these mites was begun, i.e. about the middle of June 1948, and the following method of breeding was practised with satisfactory results:—

Wild rats collected from rural areas were etherized and those found to be harbouring larval mites in their ears were placed in small wirenetting cages suspended over a dish containing water. Larval mites as they engorged dropped off and fell into the water. On the surface of water the mites could easily be detected with a lens and picked up with a fine brush. The engorged mites were transferred to tubes 3 inches by 1 inch containing about an inch or more of fine moist sterilized sand and closed with well fitting straight sided corks covered with a piece of white cotton cloth. Provided the sand was sufficiently moist, the majority passed into the first resting or nymphochrysalis stage in from a few hours to two days. The nymphochrysalis stage lasted for 7 or 8 days after which the nymphs hatched out. As soon as nymphs were found in a tube, some mosquito eggs were added; the easiest obtainable being culex egg rafts, and these were broken up before delivery into the tube. Nymphs require a fair degree of moisture for satisfactory development. When newly emerged they are cream coloured and very active. Nymphs as well as adults avoid light and always seek the shelter of any irregularity on the surface of the sand. The making of a few trenches or holes in the sand of the tubes is beneficial, as the mites hide in these places and do not endeavour to escape from the tube to such an extent as when there are no such shelters for them to hide in. Despite this, practically from every tube a certain number are lost due to being crushed between the sides of the tube and the cork.

The nymphal stage lasts from 7 to 14 or more days. Though food and moisture are equally available some seem to develop very much slower than others. It is not unusual to see the 3 stages of nymph, imagochrysalis and adult in the same tube which was charged with a batch of engorged larval mites collected on the same day. As the nymphs feed and develop they assume a distinct

brick red or dull pinkish colour in contrast to the pale yellow or cream colour of the newly hatched individual. After feeding for 7 or more days the nymph assumes a second resting stage, the imagochrysalis, which lasts for a further period of 7 days after which the adult emerges. The adults may be distinguished from the nymphs by their larger size, heavy coat of greyish hair and the folds in the integument on the dorsum of the abdomen—features distinguishable with a hand lens. Microscopically the genital organs are seen to be fully developed.

The females deposit their eggs indiscriminately—a few at a time and continue to oviposit for about 5 months. Adults grown in June are still ovipositing in December. The number of eggs or the exact time after maturation when ova are laid has not been determined yet. From a tube containing one pair of mites 158 larvæ have been collected in 28 days so that at least 5 to 6 eggs would appear to be laid each day. Larvæ may be expected in the tubes any time 20 days after adults are seen. One of the greatest difficulties experienced so far in breeding is the control of fungi, certain kinds of which smother and kill the mites; in others the powdery spores get entangled in the hairs and embarrass the adult mites leading to sluggishness and later death. Clearing of the fungus results in a considerable loss of eggs and deutova; eggs and deutova are easily obtained by suspending the fungal debris removed from the surface of the tubes in a saturated solution of sugar. Against a dark background, the eggs which look pearly white are globular with a shell which is pitted much like a miniature golf ball. The deutova are brownish in colour and irregular in shape and when examined under the microscope are seen to consist of the orange coloured larva enclosed in a membrane with the remains of the shell still attached.

The time from egg to deutovum is 7 days and from deutovum to larva 7 days in *T. deliensis*.

In the case of larvæ that are infected with rickettsia, the following method was used to control the escape of larvæ from breeding tubes during handling and manipulation.

Tubes containing adults are kept in a receptacle which in turn is placed in a large enamel iron dish containing a solution of dettol. The rim of the dish is carefully ringed with an adequate supply of soft paraffin. When tubes have to be examined for collection of larvæ and feeding, a second large dish is used with a vaseline ring just below the rim of the vessel. In the dish are three petri dishes of water—one is used for placing the tube for examination, the second contains a smaller dry petri dish on which the corks are placed for collecting such larvæ as have come up on the cork and the third contains a deep solid watch-glass with water for receiving the larval mites which are collected from the corks and sides of the tube. Although larvæ can move easily over the surface of the

water, especially if there is the slightest current of air, they move quicker on anything solid. When collected and placed in the watch-glass with water, they usually tend to bunch up together in the middle of the watch-glass from where they can be easily picked up in batches and placed on the hair of the victim to be fed on.

The technique of feeding larval mites on mice is as follows: If sufficient mites are found in a single breeding tube, a mouse enclosed in a wire gauze tube is placed in contact with the rim of the open tube for a few hours. This attracts the larvæ which attach themselves to the mouse. When large numbers of tubes and larvæ are available it is more convenient to collect the larvæ in a watch-glass as described above and place them directly on the hair of a mouse enclosed in a small wire gauze cage 4 inches by 4 inches which is placed in a dish of fine sand. The dish of fine sand and the cage are placed in a larger container with water up to a certain level. Both dishes are protected by vaseline rings.

When the single tube method is used or when small numbers of larvæ are collected and placed directly on the hairs of a mouse enclosed in a small wire mesh tube, the mouse on release (*i.e.* in 2 or 3 hours) from the tube, is transferred to a cage which is suspended over a dish of water. This is done in order that any engorged mite or unattached ones that drop off the mouse may be received in the water and collected from there. When the second method is used, *i.e.* where the mouse is left in the 4 inches by 4 inches cage on sand, the mouse is changed every 48 hours or so, because larval mites take anything from 48 hours to 4 or 5 days to engorge; and if they drop into the sand they cannot be easily recovered from there. The largest numbers drop off on the 3rd day. Mice removed from the feeding cage are kept in the same manner as infested rats for the collection of the engorged larvæ.

In white mice the larvæ seem to attach themselves to any part of the head and body and not mainly to the ears and legs as in rats and shrews. Infected mice dying within 3 days of feeding have been found with numerous larvæ attached to the outer surfaces of the ears, round the mouth and on the legs.

The colony of mites which was started in June 1948 is now in the third generation and a few mites reared in June are still alive and breeding in December.

A brief description of the different stages in the life cycle of *T. deliensis* is given below:—

1. *Egg*.—Round, pearly white in colour when seen against a dark background. The shell is pitted like a miniature golf ball. The egg stage lasts 7 days.

2. *Deutovum*.—Brown in colour with the egg-shell broken and the larvæ remaining quiescent enclosed in a membrane. This stage lasts for a further period of 7 days and then the larva emerges.

3. *Larva*.—With six legs, light or deep orange in colour, very active, feeds on vertebrate host. In the breeding tube if the superficial layer of sand is not too moist, the larvæ hide in the sand for a variable length of time. The addition of a few drops of water to such a tube makes them emerge from hiding and climb up the sides of the tube. On the vertebrate host the larvæ remain attached for 3 to 5 days and then drop off. In another day or two, they assume the next stage.

4. *Nymphochrysalis*.—A quiescent stage in which the nymph develops within the larval integument. It lasts for about 7 days.

5. *Nymph*.—With 4 pairs of legs, orange in colour like the adult, but smaller in size and with the genital organs not fully developed. Very active, lives on the eggs of insects and after 7 to 14 days assumes the next stage.

6. *Imagochrysalis*.—This stage is the second resting stage in the cycle of development. The adult develops within the nymphal integument. This stage lasts for 7 days and then the adult emerges.

7. *Adult*.—Larger in size than the nymph, has a heavy coat of greyish hair and folds on the integument on the dorsum of the abdomen. Genital organs fully developed with 3 pairs of suckers. Sexes are separate and easily distinguishable. Has four pairs of legs of which the anterior pair is larger than the others. Very active and feeds like the nymph on insect eggs.

In plate V microphotographs of the different stages in the life cycle of *T. deliensis* are given.

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TRANSMISSION OF *RICKETTSIA ORIENTALIS* BY THE BITE OF THE LARVÆ OF *TROMBICULA DELIENSIS*

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ALTHOUGH *T. deliensis* has, for some years past, been suspected to be the vector of typhus of the XK serological type in India and Malaya, experimental proof to substantiate the theory has not been obtained so far. The chief difficulty in the way of doing that was the lack of a satisfactory method for breeding mites in the laboratory and obtaining larvæ in sufficient

numbers for use in transmission experiments. The fact that it is only during the larval stage that these mites feed on a vertebrate host, necessitates the rearing of at least two generations of larvæ in the laboratory—the first generation for infecting with a known strain of *R. orientalis* and the second generation (bred out of the infected first generation) for transmitting infection by their bites to clean animals. In a previous paper we reported success in the breeding of *T. deliensis* under artificial conditions using mosquito eggs as food for the nymphs and adults. By this technique it is possible to obtain several generations of larvæ without difficulty. Using the technique we conducted transmission experiments to find out if *T. deliensis* is the vector of *R. orientalis* or not in the Barrackpore area. In 5 out of 8 experiments performed positive transmission was achieved through the bite of *T. deliensis* larvæ. Details of the experiments performed and the results obtained are given below :

Technique of infecting mites.—Larval mites originally obtained from rats in the Barrackpore area and bred out in the laboratory were used. First generation mites which were assumed to be clean were fed on mice infected with *R. orientalis* and the engorged mites dropping from the mice collected and bred out again. The larvæ coming out of these infected parents were used in transmission experiments.

The strains of *R. orientalis* used in these experiments were from two sources—human and rodent. The human strains had originally been isolated from human cases of XK typhus and subsequently maintained in the laboratory in white mice. The rodent strain was isolated from *Rattus rattus* caught in the area and identified as *R. orientalis* on the basis of serological and pathogenicity tests.

The mice used in these experiments belonged to the Haffkine Institute breed of white mice. They are susceptible to *R. orientalis* infection and, when injected intraperitoneally with an inoculum containing *R. orientalis*, live usually for about ten days and then succumb to the infection. Depending upon the dose of *R. orientalis* and the resistance of the mouse, this period varies between 6 and 15 days with an average of about 10 days.

In order to be certain that the infected mice used for feeding clean larvæ would live for at least 3 days after the larvæ had attached themselves to the mouse, infected mice which had been inoculated 4 to 6 days previously were used for the purpose. This worked well as the majority of infected mice lived long enough to enable the mites attached to them to get well engorged and drop off.

The infected engorged larvæ were collected and reared up to the adult stage and their progeny (larvæ) obtained for transmitting infection to clean mice. The progeny are infected as there is transovarian transmission of infection from

TABLE I—concl'd.

Case number	Week of the disease	WEIL-FELIX		PLASMA PROTEIN GM. PER CENT			WHITE CELL COUNT					B.P. mm. Hg.
		Type (OX)	Dilution	Total	Albumin	Globulin	Total (cu. mm.)	Poly. per cent	Lymph per cent	Mono. per cent	Eosino. per cent	
18	2	K	400	5.8	3.0	2.8	3,800	51	43	6	0	104/68
	3		400	5.5	3.2	3.3	92/56
	4			6.5	3.2	3.3	110/65
19	2	K	400	7,400	53	44	3	0	110/66
	3		1,600	
	4		800	
20	2	K	100	6.1	3.1	3.0	9,000	65	32	2	1	102/62
	3		100	
	4		200	
	5		800	
21	2	K	50	5.5	2.8	2.7	7,500	65	30	4	1	105/70
	3		200	6.2	2.5	3.7	96/55
	4		200	6.8	3.7	3.1	100/65
22	2	K	100	7,800	59	31	6	1	115/45
	3		100	125/78
23	2	K	200	12,500	83	16	1	0	85/45
	3		50	102/55
24	2	K	100	3,750	33	60	7	0	95/60
	3		100	92/45
25*	2	K	100	5.5	2.5	3.0	6,000	65	30	4	1	95/45

* Rickettsia +.

Weil-Felix reaction (vide table I).—This was done as a routine measure in every case and repeated weekly or earlier in most cases. The reaction with OX19 was positive in 4 cases (nos. 1, 2, 3 and 4), while with OXK it was positive in the rest except one (no. 13) in which the test was completely negative but *rickettsia* was demonstrated. The lowest possible dilution worth consideration is 1 in 100 which was positive in 7 cases in one of which *rickettsia* was isolated. An equal number had positive reaction in dilution of 1 in 200. The test was positive in higher dilutions in the remaining cases. Rising titre

was common and the maximum observed was 1 in 12,800 in the 4th week (no. 6). Widal reaction for typhoid and paratyphoid A and B was negative in all the cases. *Rickettsia* was demonstrated in the peritoneal fluid of mice inoculated with blood in 3 cases (nos. 13, 15 and 25).

Glucose tolerance test.—Glucose tolerance test was carried out in 10 patients with a view to studying the carbohydrate metabolism in this disease and also to see whether glucose is absorbed normally from the intestine during the fever. The results of the tests are given in table II:—

TABLE II
Showing results of glucose tolerance test

Case number	Day of disease	BLOOD SUGAR IN M.G. PER 100 ML.					URINE SUGAR (PER CENT)	
		Fasting	½ hour	1 hour	1½ hours	2 hours	Before	After
4	16	80	100	120	136	95	0	0
7	12	92	152	172	206	331	0	1.5
	30	61	164	131	93	34	0	0
12	17	90	140	115	100	90	0	0
14	18	110	120	140	120	120	0	0
16	17	120	134	161	199	174	0	1.0
17	14	90	130	120	100	86	0	0
18	13	86	130	146	120	90	0	0
21	13	70	131	113	102	70	0	0
22	17	96	130	165	180	155	0	0.8
24	19	90	130	160	150	100	0	0

From the above results it is clear that there was no impairment of the function of the intestine, so far as absorption of glucose was concerned. The test was normal in six, but in four cases (nos. 7, 16, 22 and 24) some degree of impairment of tolerance of glucose was evident. In fact, in 3 of them a diabetic type of curve was noted with appearance of sugar in the urine. In one case (no. 7) the test was repeated during convalescence prior to his discharge from the hospital and it was normal.

Plasma protein changes.—In view of the accumulated evidences from clinical and experimental observations pointing to the importance of plasma proteins in prognosis and convalescence and in the production of antibodies in acute infections, plasma protein changes in typhus fever were studied in 16 cases of this series. Total plasma proteins were estimated by copper sulphate specific gravity method of Phillip's and van Slyke and the albumin-globulin fraction by biuret method (Lowe and Chakravarti, 1946). Periodic examinations of plasma proteins about once a week during the course of the illness were carried out and in all 32 observations were made. Distribution of plasma proteins in these 32 observations is graphically shown in figure 1. When all these observations are grouped according to the weeks of the illness the results obtained are given in table III.

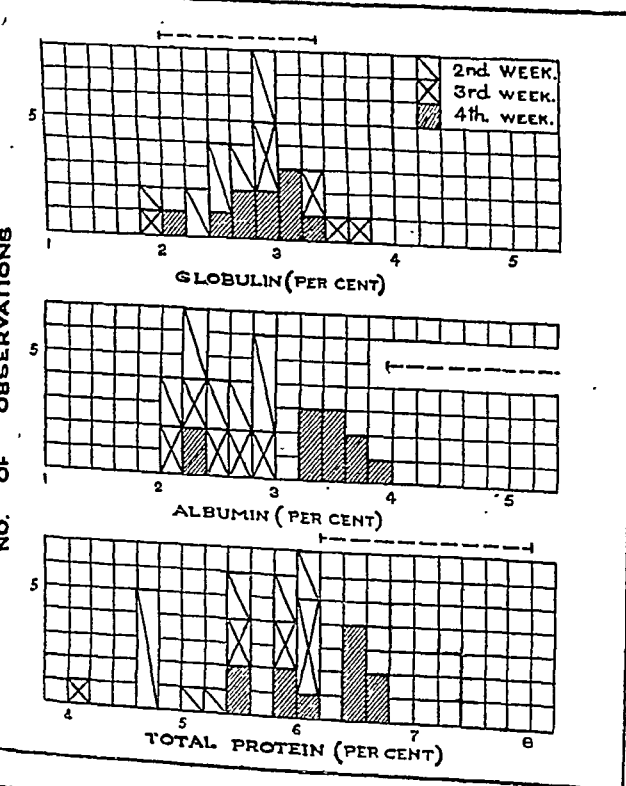


Fig. 1.—Plasma proteins of 16 patients with typhus fever (32 observations). Broken horizontal lines indicate normal limits.

From table III it is apparent that the plasma proteins are definitely reduced in this disease. The reduction is mainly due to the fall in the albumin level. The actual degree of reduction cannot be judged from the reading of the total protein alone for in the latter part of the illness the rise in globulin fraction masks the profound fall in the albumin. In the 4th week and afterwards plasma protein level tends to return to normal.

TABLE III

Week of illness	Number of observations	PLASMA PROTEINS (GM. PER CENT)		
		Total	Albumin	Globulin
2nd	13	5.28 ± 0.46	2.69 ± 0.30	2.59 ± 0.37
3rd	18	5.75 ± 0.73	2.56 ± 0.23	3.19 ± 0.61
4th and afterwards.	11	6.26 ± 0.47	3.27 ± 0.47	2.99 ± 0.35
Normal	..	7.1 ± 0.52	4.5 ± 0.37	2.6 ± 0.29

Treatment

The treatment was mainly dietetic and symptomatic. In one case para-aminobenzoic acid was used.

Diet.—The diet which was designed by us for the treatment of typhoid cases (Chaudhuri, 1948) was usually prescribed, but the actual amount of food given varied according to the patient's dietetic habits, appetite and the degree of toxæmia, etc. The diet usually supplied 2,000 to 2,500 calories per diem including proteins about 60 to 90 gm., fat about the same and carbohydrate 300 to 400 gm. This diet was maintained more or less throughout the whole course of the disease. Protein hydrolysate preparations were added to the diet in some patients who were unable to take adequate food by mouth. Vitamin supplements, particularly vitamins B and C, were given in most cases. Where the dietetic intake was insufficient plasma transfusion was given; it was particularly useful in seriously ill patients with lowered blood pressure and blood proteins. Two patients had to be fed by nasal route for a few days. Glucose-saline drip intravenously was given to the dehydrated patients. Nursing care is a very important factor in the management. Hydrotherapy, attention to the skin and mouth hygiene, regular feeding, regulation of bowels by simple enema on alternate days in constipated patients, adequate fluid intake, recording of urinary output, administration of oxygen in proper way when required are some of the special points from nursing standpoint of view. In fact, the nursing care is the same as for enteric fever.

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	30	61	164	131	93	34	0	0
12	17	90	140	115	100	90	0	0
14	18	110	120	140	120	120	0	0
16	17	120	134	161	199	174	0	1.0
17	14	90	130	120	100	86	0	0
18	13	86	130	146	120	90	0	0
21	13	70	131	113	102	70	0	0
22	17	96	130	165	180	155	0	0.8
24	19	90	130	160	150	100	0	0

loose motions. Apathy and wasting appeared. Blood pressure was 110/60. Repeated Weil-Felix reaction was negative, but *R. orientalis* was demonstrated from the inoculated mice. The temperature of remittent type continued for 15 days and then gradually became normal on the 20th day, the convalescence being uneventful. Treatment given was supportive and symptomatic.

Profound toxæmia, delirium, tremor, picking of bed clothes and insomnia. Headache moderate. Relative bradycardia and few crepitations at the base of right lung. Spleen was palpable. B.P. 118/75, temperature 104°F., respiration 40 per minute. Provisional diagnosis of typhus fever was made on admission and this was subsequently confirmed by Weil-Felix reaction and demonstration of *R. orientalis* in the inoculated mouse.

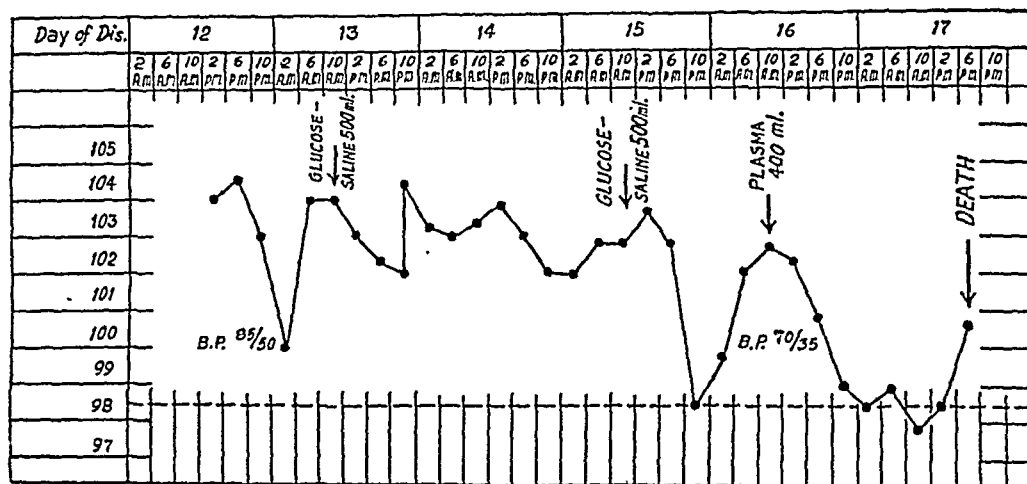


Fig. 2.—Temperature chart of case 9.

The infection was acquired in the laboratory and the infected area (cschar) was inflamed resembling a whitlow. The clinical picture was fairly typical and the diagnosis was confirmed by demonstration of *rickettsia*, while the Weil-Felix reaction was negative showing the unreliability of this non-specific test.

Case 15.—J. S., aged 22 years, male, admitted on the 8th day of continuous fever with insidious onset, sore throat, injected conjunctivæ and adenitis of the neck and groins. A gland in the posterior triangle of the neck was punctured before admission on a suspicion of plague with negative result. No rash, no eschar.

He later had broncho-pneumonic signs, ulceration of the throat and tympanitis. The blood pressure came down to 98/55 on the 15th day. The patient was practically comatose during the height of the illness. Profound toxæmia and continuous temperature persisted for the subsequent 10 days and the temperature began to fall by lysis from the 19th day, becoming normal on the 23rd day of the illness (figure 3).

Skiagram of the chest revealed diffused broncho-pneumonic mottling. Penicillin 25,000 units every 3 hours was given for the first 5 days without any effect on temperature or lung symptoms. On the 16th day of illness when the

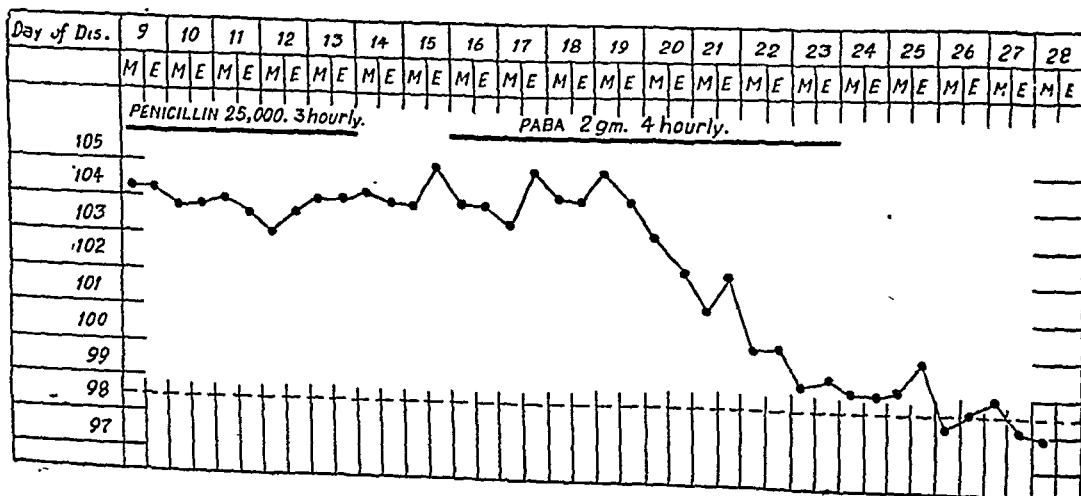


Fig. 3.—Temperature chart of case 15.

positive report of mouse inoculation was available the patient was given PABA 2 gm. 4-hourly till the temperature was normal on the 23rd day. Effect of the drug was difficult to judge from this case as it was given when the fever might as well have come down to normal by itself.

During convalescence the patient complained of slight numbness and tingling in the hands which cleared after a few injections of thiamine chloride. Wasting of the body was also marked, but subsequent progress was uneventful.

Discussion

Typhus fever has long been known to be endemic in Calcutta and its environs. Bradley and Smith (1912) reported a case in Barrackpore area which was very suggestive of typhus. Basu (1924) described 15 cases in Calcutta which he considered to be typhus. Boyd (1935) and Wilson (1935) reported a few cases in the Army apparently contracted in the Calcutta area. The diagnosis is however apt to be missed, and frequently the disease is passed as one of enteric group of fevers or pyrexia of unknown origin. Army experiences in the last war have however changed the outlook. In 1943 Lusk encountered 114 cases in an Indian military hospital. Many of the cases were not severe and the mortality rate was 14.9 per cent. No vector was identified but it was pointed out that Calcutta is an area where infective vectors are present during the second half of the year (Lusk, 1945). Sen Gupta (1944) reported a case of typhus fever complicating kala-azar. Roy (1946) gave an account of typhus fever occurring in India since 1852 and reported 2 cases occurring in South Calcutta, both of whom died. More recently, Krishnan and Smith have encountered more cases particularly in Barrackpore and made valuable contribution on the subject.

In the present series 20 cases were of mite typhus and 4 of murine typhus. Eight patients were seriously ill with 2 deaths. The rest were moderately ill and recovered often with a prolonged convalescence. The clinical features generally resembled those of tsutsugamushi fever of Japan. An acute febrile condition with headache, pains in the body, injected eyes and possibly congested throat with absence of malaria parasites in the blood should raise the suspicion of typhus fever especially if it occurs in the second half of the year. A careful inspection should be made for an eschar, lymphadenitis and rash. They are however inconstant and are apt to be missed, but if present, a clinical diagnosis is possible. Mental apathy and shortness of hearing are additional useful diagnostic points. Enteric fever is easily confused with typhus but the usual sallow face, absence of nervous symptoms in the early stage, frequent abdominal symptoms and rash (relatively few spots often missed in dark skin) are important diagnostic features; the final diagnosis however rests on laboratory findings. Dengue is often characterized by acute fever, prostration, pain, rash and

even lymphadenitis and it also occurs during the rainy season, but subsides within 7 days while leucopænia and bradycardia are common features. Other acute infection such as influenza may have to be considered in differential diagnosis. Weil's disease may be difficult to differentiate before the jaundice appears. Severe pains in the body, conjunctival injection and leucocytosis point to Weil's disease and the *Leptospira icterohæmorrhagica* can be recovered from the blood and urine by inoculation into young guinea-pigs and mice. Later agglutinins develop against *Leptospira*.

The clinical diagnosis of typhus fever should be confirmed by Weil-Felix reaction and by demonstration of *rickettsia*. The former is a non-specific test, but is helpful in diagnosis when considered in relation to clinical findings in a dilution of 1 in 100 or above, particularly if there is rising titre. But the test may be completely negative. The specific complement fixation test with *rickettsia* is not ordinarily possible.

Typhus fever as any other acute infection namely typhoid is apt to cause impairment of tolerance to glucose. This may be due to diminished utilization of sugar by tissue in general or to hepatic dysfunction causing increased gluconeogenesis. Moreover, most patients are rather undernourished and as such it is not unusual to have even a diabetic curve analogous to what is known as 'hunger-diabetes' (Hofmeister, 1890) in fasting animals. Probably toxæmia and undernutrition are both responsible for impairment of glucose tolerance which becomes normal with recovery.

Hypoproteinæmia and hypoalbuminæmia noticed in the typhus cases are somewhat similar to what was observed by us in the typhoid cases. In many cases the degree of such changes depends on the severity of illness and it seems probable that the changes are characteristic of any acute febrile condition where protein breakdown is great. Plasma proteins which are in dynamic equilibrium with tissue proteins are called upon to the contribution of the increased nitrogen requirement of the body. At first the protein reserve is exhausted and afterwards the plasma protein tends to fall as if the body is burning up its own plasma proteins. Thus the fall in plasma proteins is more marked in the second and third week of the disease. Albumin suffers most and the globulin is spared. In the third week of the disease globulin tends to rise in some cases probably not wholly due to formation of antibodies but as a result of non-specific host reaction of the body towards an infection. The changes in plasma proteins are restored to normal soon after the fever subsides. Even by feeding these patients adequately fall in the albumin cannot be prevented. Role of such rapidly developing hypoproteinæmia is not clearly understood. It may be a contributory factor in the production of the ill-understood

medical shock in the acute cases, by disturbing the circulatory dynamics.

From the present study it becomes apparent that the protein metabolism in particular is grossly disturbed in these cases and in spite of liberal feeding possible the fall in the plasma protein cannot be corrected during the febrile period. If by chance proper feeding is not practicable, proteins will be further reduced. During convalescence it is obvious that the building material for plasma protein, i.e. food proteins, must be supplied and assimilated to help in the restoration of the plasma protein pattern. If at this stage exogenous supply of protein is inadequate or delayed, deficiency in plasma proteins and tissue proteins cannot be corrected and naturally the convalescence is unduly prolonged, resulting in the use of body protein and plasma protein as fuel.

Treatment given to these patients was mostly symptomatic. There were 2 deaths from peripheral failure.

Summary

1. Incidence of typhus fever in Calcutta is reviewed. It appears that it is not uncommon in the city and its environs.
2. During the last two and a half years 25 patients were admitted to this hospital. Of these 20 were from Calcutta and the rest from outside.
3. They were all Indians except 2 Anglo-Indians. Most of them were middle-class people.
4. Eighteen cases occurred between July and October including 8 in August.
5. Seventy per cent of the patients were between 11 and 30 years. The youngest in the series was 11 and the oldest 61 years old.
6. Two patients gave history of recent similar type of fever in their families.
7. Twenty-one cases were of mite typhus (OXK) and 4 of murine type (OX19).
8. Clinical features as observed in this series, prognosis and treatment are described.
9. Occurrence of hypo-proteinæmia at the expense of albumin fraction and impairment of glucose tolerance have been observed.
10. Diagnosis and differential diagnosis have been discussed.

These observations were made in connection with an enquiry on 'Enteric group fevers' under the Indian Research Fund Association. Our thanks are due to Professor K. V. Krishnan and Dr. R. O. A. Smith of the All-India Institute of Hygiene and Public Health for isolation of rickettsia in three cases. We are also grateful to the Professor of Pathology and Bacteriology and Officer-in-charge of the Department of Diabetes and Biochemistry of the School for bacteriological examinations and glucose tolerance tests respectively.

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SEROLOGICAL TECHNIQUE (contd.)

By S. D. S. GREVAL

LIEUTENANT-COLONEL, late I.M.S.

(From the Laboratory of the Serologist to the Government of India, School of Tropical Medicine, Calcutta)

DIPHTHERIA : DIAGNOSIS, IMMUNIZATION AND TREATMENT BY IMMUNOLOGICAL MEANS

Schick test.—Forearms are cleaned with soap and water, and then with spirit (methylated spirit will do). The spirit is allowed to evaporate. 0.2 cc. of Schick test toxin (purchased ready for use) is introduced intradermally in the left forearm and the same quantity of the control fluid (the same toxin heated at 70° to 85°C. for half an hour) is introduced in the same way into the right forearm, with another syringe. In preliminary Schick test in children under 8 the control fluid may be omitted.

Results are read and recorded after (i) 24 to 48 hours and (ii) 5 to 7 days. Four types of reactions are seen :—

1. Positive (= susceptible). A flush 10 to 50 mm. in diameter appears on the left forearm. It fades during the second week and is followed by brownish pigmentation (on fair skin) and desquamation. Unsightly staining may persist for months. (For this reason the test may be done on women on lower part of the thighs.) The right side should show no reaction.

2. Negative (= immune). No reaction occurs on either side.

3. Positive-and-pseudo or 'combined' (= susceptible, subject to the explanation which follows). Flushes appear on both arms. That on the left is bigger of the two and is followed by staining of the area and desquamation. (That on the right is smaller and less persistent.)

4. Negative-and-pseudo (= immune). Flushes equal (or nearly equal) in intensity and

lumbar). While walking the right shoulder stood at a lower level compared to the left. The left arm and right leg were markedly hypertrophied as compared to the contralateral parts. The loss of terminal phalanges of the left index and little fingers was striking. The fingers were thick and sausage-shaped. The hand was fleshy. Trophic ulcers at base of left middle finger were found. Pulse was 78 per minute, regular in rhythm and volume. Liver and spleen were not palpable. No enlargement of lymph glands was detected. Urine examination revealed no abnormality.

Blood :

W.B.C.	..	9,600	R.B.C. 4,600,000
			Hæmoglobin 80%
Polymorphs	..	65%	
Lymphos	..	30%	
L. Monos	..	2%	
Eosinophils	..	2%	
Basophils	..	nil.	

Kahn's reaction of blood was negative.

Heart and lungs showed no abnormality.

Nerve biopsy and nasal smear

Biopsy of ulnar nerve, nasal swabs and scrapings from trophic ulcers at base of middle finger revealed no *B. lepræ*.

Mensuration of the limbs

Circumference at 3 inches below the tip of shoulder.—Right arm 9 inches, left arm 12 inches.

Circumference at 2 inches below olecranon.—Right forearm 8 inches, left forearm 9½ inches.

Circumference of thigh at 4 inches below anterior superior iliac spine.—Right 17½ inches, left 16 inches.

Circumference of legs at 2 inches below tibial tuberosity.—Right 11½ inches, left 10 inches.

Nervous systems

Cranial nerves.—No abnormality was found.

Motor system.—Power normal and equal in both arms and legs.

Sensory system.—Anæsthesia for touch, pain and temperature was found over the left hand, arm and trunk on left side, whole of anterior aspect and up to 12th rib at the back.

Sense of position.—Rombergism was absent. In the finger-nose test the patient showed no abnormality.

Reflexes : (1) *Upper limbs.*—Deep reflexes absent on left side while they were normal on right side.

(2) *Lower extremity.*—Knee jerk diminished on right but exaggerated on left side. Ankle jerks normal on both sides. Plantar reflex flexor on left side but absent on right side.

(3) *Abdominal reflex*—absent on left side.

(4) *Cremasteric reflex*—absent on left side.

Photographs

Figure 1, plate VI, shows hypertrophy of left arm and loss of phalanges mentioned above.

Figure 2, plate VI, shows the same as figure 1 plus prominence of left side of forehead and cheek. The photo does not give a good view.

Figure 3, plate VI, shows scolioses of dorso-lumbar region and prominence of left side of chest.

Hypertrophy of right leg is also seen.

X-ray findings

Skull.—Antero-posterior and lateral views showed no bony changes or difference in size (figures 4 and 5, plate VI).

Arms.—All bones of left side are hypertrophied compared to those on the right (figures 6 and 6a, plate VII). Left humerus, radius and ulna bigger as compared to those on the right.

Legs.—All bones on right side hypertrophied compared to those on the left. Right knee bones slightly bigger (figures 7 and 8, plates VII and VIII).

Comments

In this case there was loss of sensibility to touch, pain and thermal stimuli over the left upper extremity which also showed hypertrophy. These sensations were also absent over the left side of trunk, but contralateral parts on the right side escaped—the distribution being asymmetrical. The left half of the face although it appeared hypertrophied showed no anæsthesia.

Again in contrast with the upper extremities and trunk, the right but not the left leg showed hypertrophy, i.e. the hypertrophy was on the opposite side, the lower extremity showed no anæsthesia.

Pain was found over the left olecranon region and was persistent and obstinate. To remove doubt whether the parts hypertrophied were really so or appeared so by the other side being atrophied, a very careful examination was made keeping this in mind but there was no evidence of atrophy and the parts not hypertrophied were normal in all respects. There was no atrophy of tongue.

Spinal curvature was present in the form of scoliosis with upper convexity of dorsal region to the left.

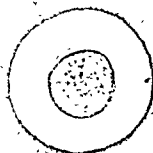
Thickening of bone of left arm and right leg were seen but no osteoporosis, the subcutaneous tissues and skin were found thickened. Fingers of left hand were sausage-like and the hand appeared fleshy.

The points of interest in this case appear to be asymmetry of hypertrophy, and the fact that while the left arm presented a suggestive picture of syringomyelia, it was the right leg which was

PLATE V

THE BREEDING AND MAINTENANCE OF *T. DELIENSIS* IN THE LABORATORY FOR
EXPERIMENTAL PURPOSES : K. V. KRISHNAN, R. O. A. SMITH, P. N. POSE, K. N. NEOGY,
B. K. GHOSH ROY & M. GHOSH. (O. A.) PAGE 39

LIFE CYCLE OF *T. DELIENSIS*.



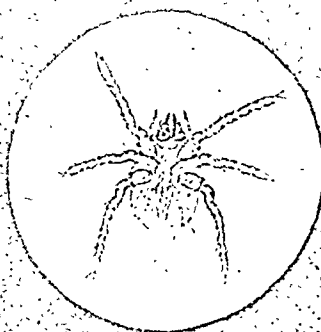
EGG



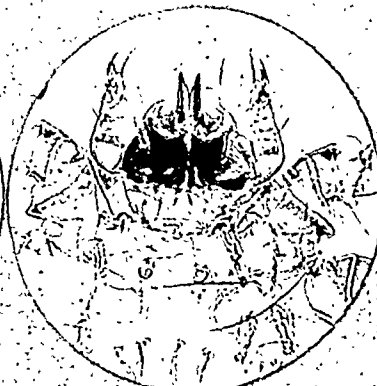
DEUTOVUM



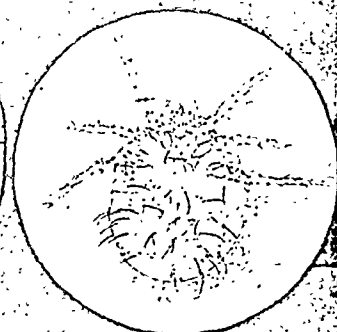
DEUTOVUM



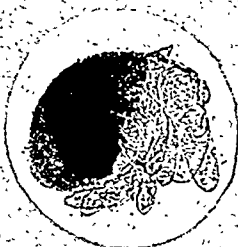
LARVA - UNFED



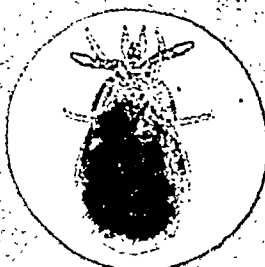
CHETOTAXY



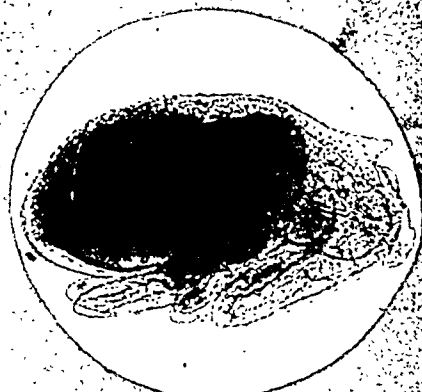
LARVA - FED



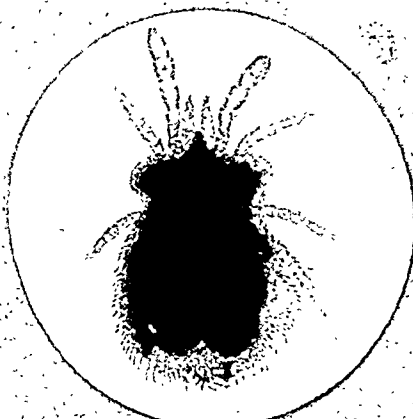
NYMPHOCHRYSALIS



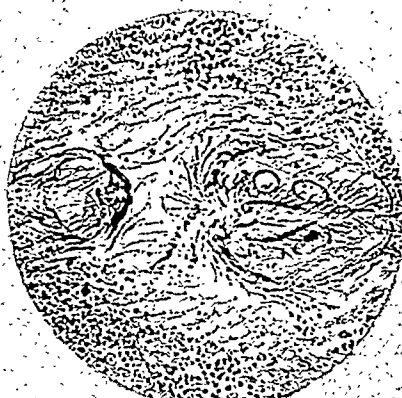
NYMPH



IMAGOCCHRYSALIS



ADULT



MALE GENITALIA



Fig 1.



Fig. 2.



Fig. 4.

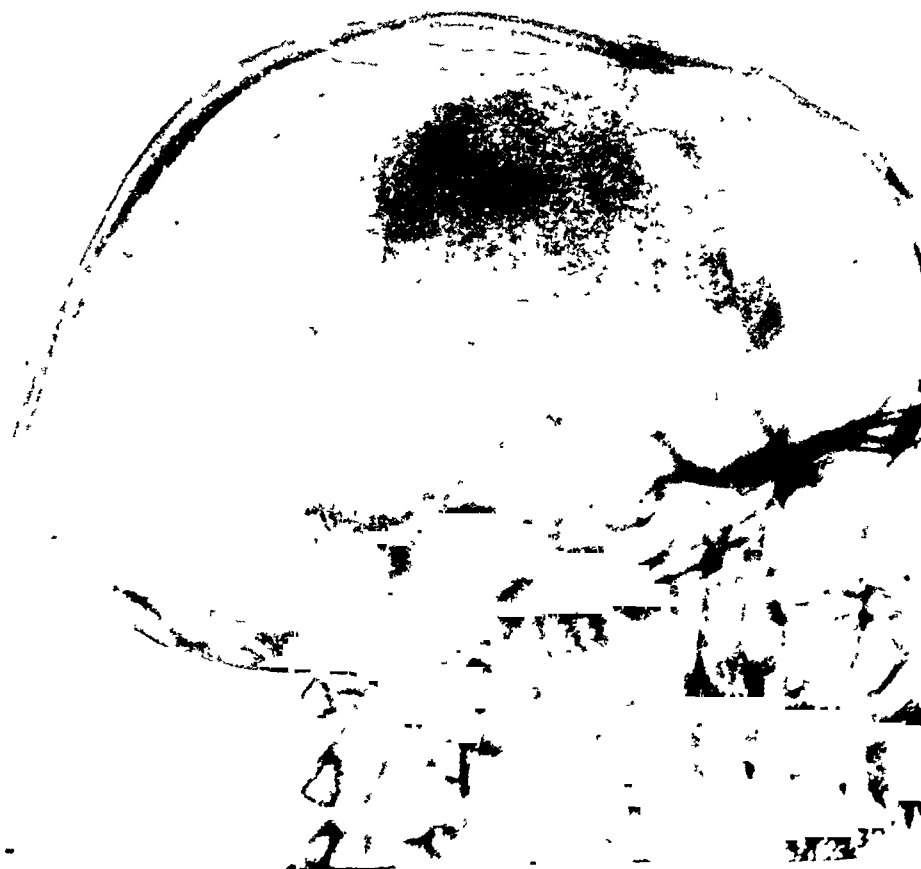




Fig. 6.



Fig. 6a.

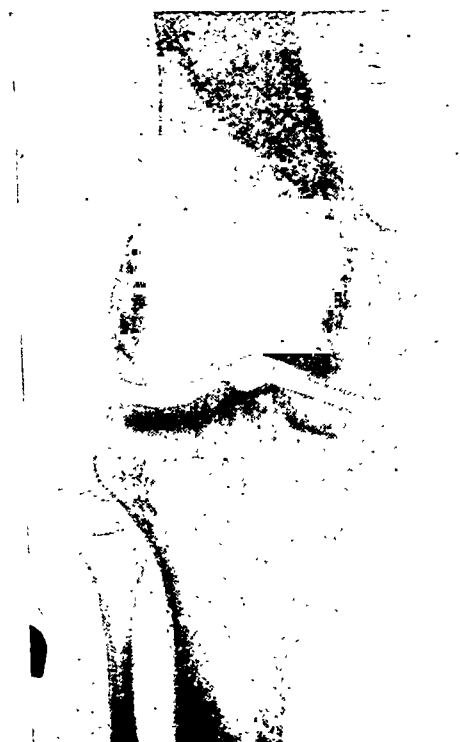


PLATE VIII

A NEUROLOGICAL CASE FOR DIAGNOSIS : GURBUXSH SINGH. (M. H. P.) PAGE 53

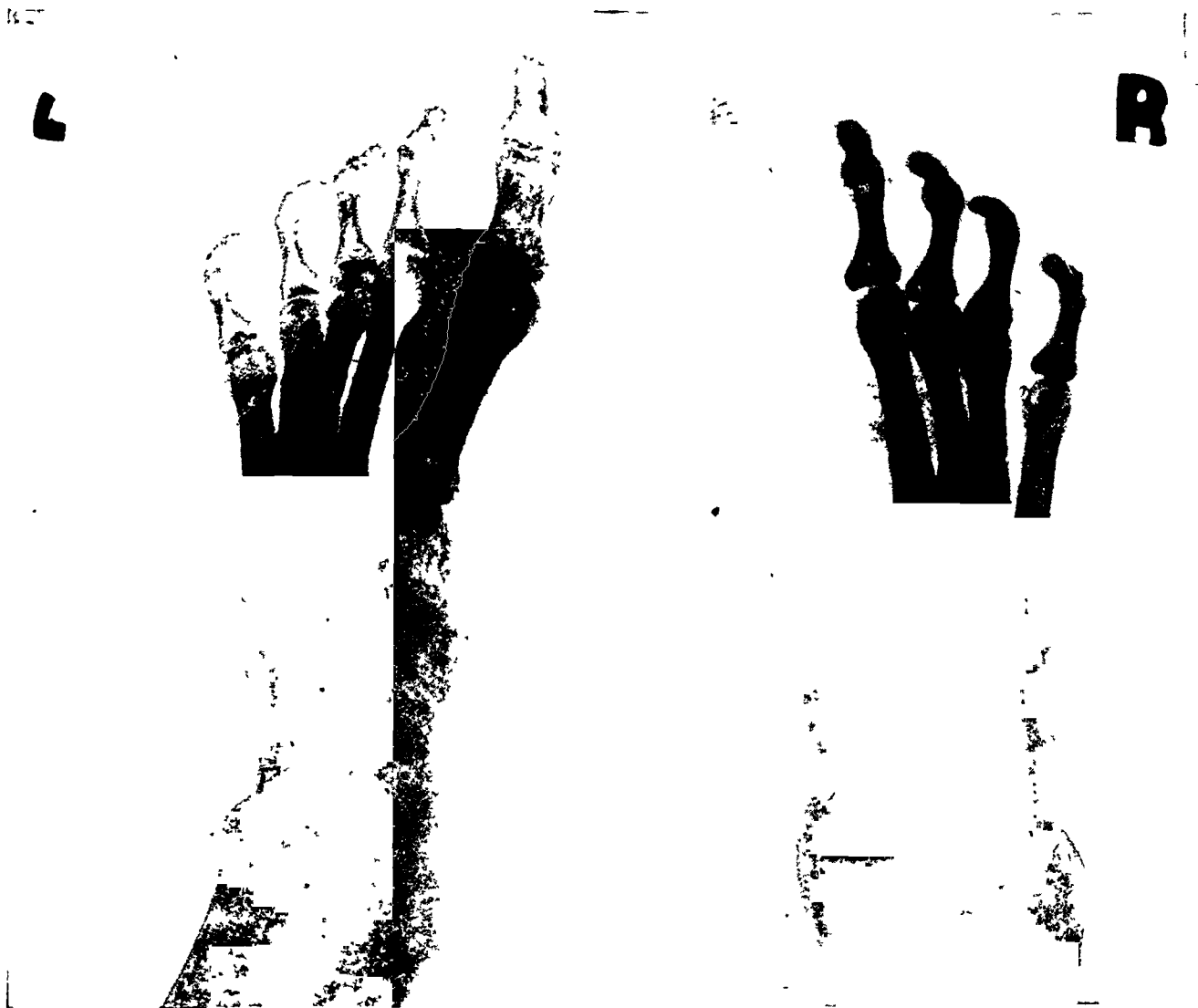


Fig. 8.

hypertrophied but showed no evidence of anaesthesia. The onset of anaesthesia took 14 years to manifest after commencement of hypertrophy. The patient was discharged from the hospital on his own request, but follow-up will be conducted to watch the appearance of anaesthesia in the right leg, or complaint of numbness.

Summary

A case for neurological diagnosis is described showing the following particularities :

1. Although the anaesthesia was complete, only the left arm was involved which showed great hypertrophy of bones, subcutaneous tissue and skin.

2. The left side of face was hypertrophied involving the subcutaneous tissues and skin but there was no anaesthesia.

3. Although the face, arm and trunk were affected on the left side, it was the right leg which showed hypertrophy of bones, subcutaneous tissue and skin, but there was no anaesthesia.

4. The hypertrophy of right leg has existed for the last 18 years without the appearance of anaesthesia which in the case of left arm followed 16 years after the appearance of hypertrophy. The numbness followed 4 years after the hypertrophy.

A CASE OF INFANTILE DIABETES MELLITUS

By S. RAJU AYYAR

Civil Assistant Surgeon, Tirukalikundram

RAMAKUMAR, a male child, 14 months old, was brought to me by his parents for rapidly deteriorating health. History revealed that this was the twelfth child born with apparently good health. For the past few months the child refused any feed and gradually grew thinner and thinner until he became skin and bone. Further, it was also learned that the mother has been ailing from diabetes. There was no other history of any peculiarity in family. The child suffered from constipation necessitating frequent glycerine enemata to clear the bowels.

On physical examination the temperature of the child was 99°F. Tongue was slightly reddish. No enlargement of spleen or liver or any superficial gland was found. Anterior fontanelle was not well closed. In the heart there was nothing abnormal excepting slight rapidity. The child was very peevish and did not permit thorough examination. A provisional diagnosis of avitaminosis (acute rickets) was made and the child was put on haliverol, cod-liver oil inunction, Parish chemical food, etc.

This line of treatment even after a fortnight did not show any improvement and I had again to visit the child in the house. I found that the

child was sleeping in a country cloth 'hanger' with a big plate kept on the ground underneath it evidently to catch the urine. When I looked into the plate, I found the urine collected disproportionate to the child's age. The specific gravity was 1040, and sugar and acetone bodies were present. This altered my diagnosis and I straightway put the child on insulin half a cc. (40 units strength) twice a day with plenty of glucose added to the feed. The urine was subsequently examined the next day and found to contain 6 per cent of sugar. The child was also given trypsin tablets thrice a day. In a week's time the child's appearance changed and he began to take interest in the surroundings asking for regular feeds but dreaded the injection needle. For four months insulin was continued daily altering only the preparation from one to another and now it is being given once or twice a week as the necessity demands. Trypsin alone is being continued daily. The present weight of the child is 14 lbs. and he looks quite normal in every other way.

This case is of interest because of its rarity. Even in Joselyn series of cases, 4 per cent are below 20 years in age and no mention is made of infants. It also gives a warning that neglect of routine examination of urine even in infants will land one into error.

[Further reports on this child are indicated.—Editor, *I.M.G.*]

Therapeutic Notes

NOTES ON SOME REMEDIES

XXVI.—DRUGS IN HELMINTHIC DISEASES, Part I
By R. N. CHAUDHURI, M.B., M.R.C.P., T.D.D. (Wales)
Professor of Tropical Medicine, School of Tropical Medicine, Calcutta

THESE drugs known as anthelmintics are effective against most of the common intestinal worms, but have a very limited scope in infections caused by worms which live in the blood or other tissues of the body. They are more or less injurious to all living matter, and their use is rendered possible in the case of intestinal parasites by slow absorption from the intestine which permits of their acting on the parasites in maximum concentration while exerting a minimum effect on the host. It is this toxicity which makes them unsuitable for tissue parasites except in the case of antimony compounds which are efficient in schistosomiasis and probably so in filariasis when given parenterally but for the sake of safety they must be administered in very small doses. The new remedy hetrazan for filariasis, which is taken by mouth, is still in experimental stages.

Drugs in use

1. *Santonin*.—It is a specific, though an expensive one, for the common roundworm, *Ascaris lumbricoides*, but it is now rated as not so effective as was once thought. It has an irritant effect on the parasites which, in trying to escape, migrate to the colon from which they are expelled by a purgative. It is customary to prescribe it as a powder (dose 1 to 3 grains) mixed with calomel which is given at bed time. 'Calomel stimulates the flow of bile which enhances the toxic action of santonin on the parasites' according to Chopra. The drug has little or no action on other intestinal parasites.

A certain amount of absorption often occurs in the intestine, causing yellow vision (xanthopsia) and yellow urine. These pass off in a few hours. Santonin is a poisonous drug which should be used cautiously in infants who are more susceptible to it than adults; even small doses may prove toxic. In severe cases of poisoning it may cause diarrhoea, hæmaturia, headache, blindness and even epileptiform convulsions.

2. *Oil of chenopodium*.—This is an effective anthelmintic particularly against ascaris and hookworms; it is also useful in whipworm infection but is a toxic drug. Owing to its toxicity a dose of 1.5 cc. instead of the maximum dose 3 cc. is recommended; this should be given in gelatine capsules in two lots at an interval of half an hour. Chopra says that the drug is less toxic and its anthelmintic effects are not only as good but better if the preliminary fasting and purging are omitted. But a purgative should always be administered later, not only to expel the worms but also to wash the unabsorbed portion of the drug out of the intestine. It should not be repeated for two weeks. The full therapeutic dose may cause gastro-intestinal irritation, and a larger dose may bring about nervous symptoms, e.g. headache, dizziness, blurred vision, stupor and collapse. There may be albuminuria and hæmaturia. These toxic effects may be delayed in their appearance for two or three days or even longer. Damage to the liver and kidneys usually accompanies these symptoms. The drug is contra-indicated in hepatic cirrhosis and respiratory and kidney disease, and should not be prescribed for small children and pregnant women. Alcohol and fats facilitate its absorption from the stomach and intestines and should be withheld during treatment.

Oil of chenopodium is often adulterated and its active constituent, ascaridol, varies in different specimens, so a reliable product should be used.

3. *Carbon tetrachloride*.—It is a colourless chloroform-like liquid which is most effective against hookworm and tapeworm infection, though to a less extent in the latter. The dose is 3 cc. which can be given in capsules or conveniently shaken up with milk or a saline purgative.

Carbon tetrachloride is a highly toxic drug and its toxicity is further increased by the impurities it often contains and by giving alcohol and fatty substances during treatment, as these increase absorption from the intestinal tract. (N.B.—It should be kept in dark and tightly stoppered bottles as poisonous substances are formed on exposure to light and air.) An hour or two after a therapeutic dose there may be headache and drowsiness. Severe cases may show nausea, vomiting, hæmatemesis, coma and convulsions. The toxic action is exercised mainly on the liver which undergoes fatty infiltration or even degeneration and necrosis. Next to the liver, the kidneys are most severely affected. The lesions may be extensive enough to cause death. The drug is contra-indicated in hepatic cirrhosis and nephritis, alcoholism, heart and pulmonary affections and pyrexia and in patients having serum calcium deficiency, as this seems to favour acute intoxication. It is not suitable for small children.

In using this drug preliminary starvation is dangerous. Patients should be placed on a high carbohydrate and protein and low fat diet, and forbidden to have any alcohol some days prior to therapy. In cases of malnutrition, preliminary treatment with diet and with calcium lactate or gluconate in full dose should be given. The day previous to treatment a light evening meal is ordered. Preliminary purgative is not required. After its administration, later, if the bowels do not move, the dose of salts is repeated or a warm enema is given to empty the bowel.

Carbon tetrachloride is not only not effective against ascaris but has an undesirable effect on the worms, viz that of increasing their activity so as to cause them to migrate to other sites or even block the intestine. So if it is used in mixed ascaris and hookworm infection, it should be combined with a small dose of oil of chenopodium which effectively disposes of the worms. (N.B.—In view of safer and equally efficient drugs being available, oil of chenopodium and carbon tetrachloride are not much used nowadays especially for ascaris and hookworm infections.)

4. *Tetrachlorethylene*.—It is a heavy non-irritating liquid with low toxicity and is the drug of choice in the treatment of hookworm infection uncomplicated with ascariasis. The dose is 4 cc. which is well shaken up in two ounces of saline purgative and given immediately to the patient; this gives the draught an even diffusion which makes it more efficient against the parasites. Or it may be given in capsules or with sugar followed later by a purgative.

In the absence of alcohol and fatty substances there is very little absorption from the intestine. The only ill effects noticed are transient burning sensations in the stomach, slight nausea and giddiness.

The remarks about the effect of carbon tetrachloride (see above) upon ascaris apply also to tetrachlorethylene.

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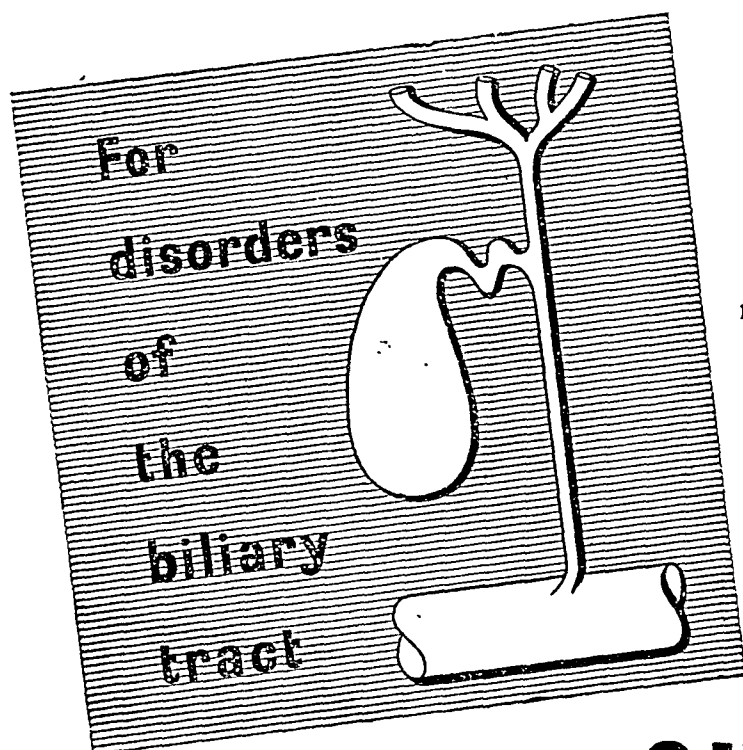
certain beef preparations. One of the substances investigated was Bovril.

As a result of these experiments (described in detail in the *British Medical Journal* of August 28th, 1937) Bovril emerged as 'the most effective stimulant.' Briefly, it was proved that Bovril increased the supply of gastric juices where there was a deficiency and restored it to normal. It is an accepted medical fact that people of sedentary habits generally suffer from a lowering of the essential gastric activity; Bovril rectifies this and, by facilitating the digestion of proteins, enables full nourishment to be gained.

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Indian Medical Gazette

FEBRUARY

TYPHUS FEVERS

WHILE the classical typhus fever is now a matter of almost ancient history in medicine, other forms of this group of fevers have been recognized within the last 20 years or so. The latest information about the latter was obtained during the World War II only. It was of military importance and remained a hush-hush affair so far as the general, non-service, medical profession was concerned. Details have been released only recently and have appeared in books (War Office, 1946; Rivers, 1948; Stitt, Clough and Branham, 1948; Gradwohl, 1948).

Twelve Fevers, their Nomenclature, Causal Agents, Vectors, etc.

The group has been divided into 12 fevers named and described as follows:—

1. *Classical epidemic typhus*.—The causal agent is *Rickettsia prowazeki*, louse borne. The synonyms are jail fever, camp fever, war fever, famine fever, ship fever, hospital fever, petechial fever, morbus hungaricus, *typhus historique*, *typhus exanthematicus*, *detoypho*, *tabardillo* and fleckfeber. There are at least 14 names.

The only items to which attention has been drawn recently are: (1) The mind of the patient is really far from inactive; the 'imagination conjures up the most frightful fancies to which implicit belief is attached, and of which a distinct recollection may remain after recovery' (Murchison, 1862, quoted by Rivers, *loc. cit.*). (2) The electron microscope reveals that rickettsiæ, like vaccine virus and bacteria, appear to have a limiting membrane surrounding the protoplasm in which are embedded granules. (3) Macchiavello's method of staining is the most satisfactory method for rickettsiæ. Smears are (i) fixed lightly by heat, (ii) stained for 3 to 5 minutes with 0.25 per cent basic fuchsin in distilled water, (iii) dipped quickly in 0.25 to 0.5 per cent citric acid in distilled water, (iv) placed in running tap water, (v) flooded with 1 per cent methylene blue in distilled water for a few seconds, (vi) washed briefly in running tap water, and (vii) dried with filter paper. (4) About 10 per cent of cases and many experimental animals do not develop agglutinins for proteus OX19. (5) There is no evidence of a true exotoxin produced by the rickettsiæ. (6) Infection with *Proteus vulgaris* will of course produce agglutinins, and some subjects may have them naturally without any known cause. The titre in these cases will be constant. (7) The diag-

nistic titre is 1 in 160 but a rise in titre from 1 in 20 or 1 in 1 is significant (Rivers, *loc. cit.*). Even a titre of 1 in 100 may be accepted (War Office, *loc. cit.*). (8) Para-amino-benzoic acid given in the first week of the disease has a favourable influence on the course of the disease. (9) DDT dusting powder will kill all lice on a patient. The dusting is repeated after a week. (10) A subject recovered from classical typhus is immune to the murine typhus and *vice versa*.

2. *Murine typhus*.—Its causal agent is *R. mooseri* which is borne by the rat-flea, *Xenopsylla cheopis* (the same species which carries plague). The synonyms are endemic typhus, urban typhus, shop typhus of Malaya, flea typhus and rat typhus: there are at least 6 names.

The causal agent is capable of causing an epidemic after a few passages through human lice and is serologically indistinguishable from *R. prowazeki*, the serum of the patient reacting with OX19 similarly.

The agent multiplies in the gut of the flea without harming the insect (the louse is harmed by the agent of the epidemic typhus) which continues discharging it in its faeces.

From rat to rat the agent is carried by the same flea and by rat louse *Polyplax spinulosus*. The infected rats can impart infection to man by infecting food with their urine. A human case cannot transmit the disease to other persons direct.

The disease is milder than the epidemic typhus and has been reported recently from Bombay (Soman, 1947) and Calcutta (Lowe, 1946; Krishnan *et al.*, 1949; Chaudhuri and Chakravarti, 1949).

3. *Brill's disease*.—The present opinion on this form of typhus fever is that it is a recrudescence of the epidemic typhus in a subject who had it previously. Such a patient can start an epidemic. The causal agent resembles that of the epidemic typhus and not of the murine typhus. In America the nomenclature of Brill's disease is used for fever found in immigrants from Europe only. Further observations on the recrudescence are necessary.

4. *The spotted fever of Rocky Mountain of America*.—The causal agent is *Dermacentor rickettsi*, also known as *Rickettsia rickettsi*, *R. brasiliensis* and *R. typhi*. It is tick borne and about a dozen ticks have been incriminated under the leadership of *Dermacentor andersoni*. The infection is trans-ovarian. This is contracted in the forest by small rodents or other mammals.

The other names are mountain fever, typhomalarial fever, bull fever, black fever, blue disease spotted fever, Sao Paulo mural typhus, Minas Geraes fever and Tobia fever. There are at least 9 names.

The differential agglutination has been mentioned under every fever and may be summarized as follows:

Disease	Reaction
1. Classical epidemic typhus	OX19 ++++ OX2 + OXK -
2. Murine typhus ..	OX19 +++ OX2 + OXK -
3. Brill's disease ..	OX19 +++ OX2 + OXK -
4. Rocky Mountain spotted fever ..	OX19 ++ OX2 + OXK ++
5. Boutonneuse fever ..	OX19 ++ OX2 + OXK ++
6. South African tick bite fever ..	OX19 ++ OX2 + OXK ++
7. Rickettsial pox ..	
8. North Queensland tick typhus ..	OX19 - OX2 - OXK -
9. Tick bite rickettsial fever in India ..	
10. Tick bite rickettsial fever in Russia ..	
11. Scrub typhus ..	OX19 - OX2 - OXK +++
12. Trench fever ..	OX19 - OX2 - OXK -

These reactions are based on Topley and Wilson's *Principles of Bacteriology and Immunology*, 1946, *Memoranda on Medical Diseases in Tropical and Sub-tropical Areas*, 1946, Stitt's *Practical Bacteriology, Hematology and Parasitology*, 1948, and Gradwohl's *Clinical Laboratory Methods and Diagnosis*, 1948. Regarding the relative intensity of the reaction the agreement is not perfect. Even nomenclature of the fevers varies slightly. Sao Paulo rural typhus of the Memoranda, for instance, is merged into the Rocky Mountain spotted fever of Stitt.

The results of Weil-Felix test should be correlated with the clinical findings. The reaction has been found positive in the course of other diseases like undulant fever, enteritis, typhoid fever and dysentery (Wilson and Miles, *loc. cit.*).

In scrub typhus the mouse infection test ultimately appears to establish the diagnosis. Ascites is a constant feature and smears from the peritoneum are positive. All infected mice, however, do not sicken. Guinea-pig scrotal reaction provides the distinction between this form of typhus and others. Typically the swelling is deep in murine typhus, superficial in Rocky Mountain spotted fever, absent in scrub typhus and usually absent in classical typhus. For inoculation washed rbc suffice. Rats and mice can harbour the infection in brain only.

The use of OX2 does not appear to be very helpful on the whole.

In the war laboratories, rickettsial agglutination tests with the antigens themselves have given differentiation between epidemic and murine typhus, a differentiation not possible with Weil-Felix reaction. The preparation of the antigens however is not easy. When standard antigen suspensions are available for all rickettsial infections more definite diagnosis and inter-relationship between the infections will be possible. Complement fixation will also be possible with suitable antigens, although in endemic areas it is not likely to give much information. Presumably normal individuals in endemic areas in the U.S.A. have given strong reactions in weak dilutions of their sera (Johnson and Damson, 1946).

A Point in Epidemiology

It appears quite possible that scrub typhus has been introduced into India recently, *after* the World War I and *during* the World War II: Otherwise spread of 'fever' from Hindu places of pilgrimage would have attracted attention. Nearly half such places are situated in jungles. No such spread has ever attracted attention. In the past PUO in the Army in India has not been associated with manœuvres and bivouacs. Whether the fever now detected will thrive or die out the next few years will show. The fact of its dying out will lend support to the view of recent introduction.

If the disease fails to thrive it will not be the only disease so affected. Adverse tellural influence in India on the causal agents of many diseases which cripple and kill elsewhere is striking (Greval, 1946).

When suitable soluble antigens are available, it will be possible to look for endemicity by examining sera routinely by complement fixation with these antigens from samples left over after the Wassermann reaction.

Other Rickettsiae

There are rickettsiae other than those responsible for human diseases. Some cause diseases in animals, others live in arthropods, with or without causing inconvenience to the hosts.

An Allied Micro-organism

Bartonella bacilliformis, the causal agent of Oroya fever and verruga peruviana, is such a micro-organism. It has been considered 'closely similar' to rickettsiae and 'rickettsia-like' (Hyman, 1946; Pinkerton, 1947).

Another Micro-organism requiring Special Condition for Growth

Donovania granulomatis, the causal agent of granuloma venereum, is such a micro-organism. Its primary culture succeeds only in the yolk sac of a developing chick embryo.

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Medical News

BRITAIN CREATES THREE HEALTH RECORDS

(From Release No. B.F. 269 issued by the British Information Services, New Delhi)

BRITAIN set up three new health records in 1948. Figures just published by the Registrar-General show that death rates in Britain are now the lowest ever known. In addition to a spectacular fall in the general death rate fewer babies died and the number of still-births was the smallest ever recorded.

Commenting on these figures a representative of the Ministry of Health spoke of these records as remarkable. 'They mean that the death rate among infants in their first year of life fell last year by 17 per cent compared with the previous lowest rate. The rate has been almost halved since 1941 when it was 60 per 1,000 births.'

There were 26,600 deaths of children under one year in 1948, giving a mortality rate of 34 per thousand. This is the first time that the annual rate has fallen below 40, the previous lowest being 41 during 1947.

The total number of deaths registered in England and Wales was just over 470,000. This is the lowest for 18 years although the population increased by 3,500,000. It represents a record low death rate of 10.1 per 1,000.

The birth rate continues to be substantially higher than before the war. Live births registered last year in England and Wales were more than 777,000. This compared with a pre-war level of 621,000 in 1938.

Another record announced by the Ministry of Health is the lowest known number of deaths from diphtheria during 1948.—(London Press Service.)

WAR AGAINST MALARIA TO BE INTENSIFIED

THE Government of India, it is learnt, are to intensify their campaign against malaria during 1949.

Arrangements have been made with the World Health Organization for four expert demonstration malaria teams to arrive in India shortly for field work.

With a view to cover the entire field of malariology, including latest researches, it has been decided that the six-week malaria course at the Malaria Institute of India should be extended to twelve weeks and that the number of lectures should be increased to 75 and practical work to 275 hours.

The first expanded course, which is to commence on 7th February, will include practical demonstration of field work in hyperendemic areas in the United Provinces and visits to irrigation and multi-purpose projects. Twenty seats for the course are allotted to Indian candidates and six to foreign candidates.

AUSTRALIAN HOSPITAL INVENTIONS LIGHTEN NURSES' TASKS

By LEN BARKER

(From Release No. P/1033 issued by the Public Relations Officer, Australia Office, New Delhi)

THREE inventions designed to minimize much of the manual work in hospital nursing and to facilitate certain forms of medical treatment have been developed in Australia by the engineering staff of Melbourne's Austin Hospital for Cancer and Chronic Diseases, under Mr. E. O. Cartwright, Chief Engineer.

Mr. Cartwright has already achieved international recognition for the development of a water-powered 'iron-lung'.

The latest contributions to medical progress of the hospital's engineering section are a 'hoist-bath', an apparatus for lifting patients, and a cot fitted with an elevating floor which can be raised or lowered by a simple action.

Of the three inventions, perhaps the most important is the hoist-bath. Operating on much the same principle as the hydraulic garage hoist used to raise automobiles, the hoist-bath has an elevating platform which can be raised or lowered in the bath. The platform actually forms the bottom of the bath. Although it was specifically designed for non-ambulatory patients with chronic diseases, it can be applied to all types of patients who are difficult to bathe in plunge baths because of the handling involved.

With the hoist-bath, the patient can be wheeled to the side of the bath and moved gently and easily from the trolley to the platform, which then descends slowly under the patient's weight. The bath is filled from a thermostatically controlled water supply.

When bathing is completed, the patient is raised to trolley level simply by depressing a lever.

The medical staff at the Austin Hospital say that the hoist-bath has taken all the hard work out of the formerly 'backbreaking job' of lifting patients in and out of a bath. In addition it has made bathing possible for patients who, because of obesity or other causes, could not be lifted by hand.

In the original design, the hoist was planned to operate direct from the water mains. However this had to be discarded after the authorities controlling Melbourne's water supply forbade it on the grounds that the mains might be in danger of pollution from the bath.

They pointed out that since the ram of the bath would come in contact with both the bath water and the fresh water supply there was a possibility of contamination through syphonage.

The design was modified, and the ram was actuated by oil compressed in a small tank by an electric pump. Although this design operates smoothly it has the disadvantage of being very noisy due to the stainless steel of the bath acting as a sounding board for the electric motor.

In addition, some medicos were unhappy about the proximity of a source of electricity to the bath.

To meet these objections, the design has again been modified.

Mr. Cartwright has reverted to the original design by using the water main as the primary source of power. The water drives a pump which in turn compresses oil to actuate the ram. In this way, the various faults of both the earlier designs have been eliminated.

Patient-lifting.—Second of the inventions—the 'patient-lifting apparatus' not only is a work saver but has a particular value in the treatment and handling of orthopaedic patients.

In appearance this apparatus is not unlike a set of boat davits. Mounted on wheels, the stainless-steel framework supports five adjustable canvas straps which can be easily slipped under the patient. The straps are attached by wires to a set of pulleys. The patient is lifted by an expanding pulley powered by a one-ton automobile jack, which can be operated with the minimum of effort by a nurse.

Medical men who have inspected the apparatus say that it will be of particular use for patients who are suffering from debilitation, paralysis, joint-disease or obesity. It means that they can be easily transported around the hospital or moved while their beds are being made.

The third invention was designed for children's wards at the hospital, which treats, among other chronic diseases, infantile paralysis.

In this invention the standard 'drop-side' cot has been done away with by the construction of a cot with an elevating floor which can be raised flush with the top rails by a scissors-spring arrangement. The bottom

of the cot is raised or lowered simply by moving a lever.

The cot has been found greatly to facilitate medical examinations, while nurses are saved much of the work normally attached to caring for their small patients.

RADIO-ACTIVE ELEMENTS AID MEDICINE AND INDUSTRY

(From Release No. B.F. 386 issued by the British Information Services, New Delhi)

BRITISH scientists have established that by mixing radio-active atoms of phosphates with ordinary fertilizers, it is possible to see how the plant uses the fertilizer with which it is fed. By mixing radio-active carbon dioxide with ordinary carbon dioxide, one can study the method by which plants turn carbon dioxide into food under the influence of sunlight.

In the same way, with radio-active and ordinary iodine, it is possible to trace where the iodine is going to when treating the thyroid gland. Radio-active phosphorus can be used to determine the volume of blood in the body, and also for testing how the body utilizes blood.

Radio-active elements can help industry in many ways. In the oil industry a little radio-active carbon introduced into crude oil enables it to be followed in its wanderings round the chemical plant. Metallurgists are making increasing use of this process in studying the rate at which bearings are being worn.

By means of the atomic pile new elements which have not existed on the earth before can be produced.

PSYCHO-ANALYSIS TO COMBAT JUVENILE DELINQUENCY

(From Release No. B.F. 381 issued by the British Information Services, New Delhi)

GREATER London Councils are setting up guidance centres to psycho-analyse children. It is felt that many children can be helped by much treatment and that it may eventually reduce juvenile delinquency.

A centre to be opened at Hayes, Middlesex, covering an area with a school population of 33,000, will include on its staff a psychiatrist, a psycho-therapist, an educational psychologist and a clerk.

NOBEL PRIZE IN MEDICINE FOR 1947

(From the *United States Naval Medical Bulletin*, Vol. 48, January-February 1948, p. 98)

THE recipients of the Nobel Prize for Medicine and Physiology were announced on 23rd October by the Karoline Medical Institute, Stockholm, Sweden, charged with the award. They are Dr. Carl F. Cori and his wife, Dr. Gerty Theresa Cori, of Washington University, St. Louis, and Dr. B. A. Houssay, Chief of the Institute of Experimental Biology and Medicine in Buenos Aires, Argentina.

Dr. and Mrs. Cori received the award for their work on sugar metabolism, particularly the effects of the enzyme which converts starches to glycogen.

Dr. Houssay's work was on the relation of the pituitary controls of sugar metabolism so that the results of all three investigators have a most important bearing on the biochemistry and treatment of diabetes.

The cash value of the prize this year amounted to 175,115 Swedish crowns or \$48,921. The Cori's received one-half or \$24,460.50 and Dr. Houssay an equal amount. Dr. Cori is 51 years of age, Dr. Houssay 60. The former has an 11-year-old son, the latter three sons who are physicians.

Public Health Section

EPIDEMIOLOGICAL OBSERVATIONS ON XK OR MITE-BORNE TYPHUS IN BARRACKPORE, BENGAL

By K. V. KRISHNAN

R. O. A. SMITH

P. N. BOSE

K. N. NEOGY

B. K. GHOSH ROY

and

M. GHOSH

(From the Bengal Typhus Enquiry at the All-India Institute of Hygiene and Public Health, Calcutta, partly financed by the I. R. F. A.)

In the course of investigations on typhus conducted in the cantonment town of Barrackpore by the Bengal Typhus Enquiry, between 1946 and 1948, certain data relating to the epidemiology of the disease were collected and in this article a brief account of the observations made and conclusions arrived at are presented.

Review of available information on epidemiology of XK typhus in other areas

This disease was first recognized in Japan about 1878. When reports about the disease were published in the medical press, other countries became alive to the possibility of this fever occurring among their people. Between 1909 and 1935 many scattered endemic areas were found in China, Indo-China, Dutch East Indies, Australia, Malaya, Burma, India, and several islands in the Far East. In these areas the disease is now known to be responsible for a fair amount of morbidity and for a variable amount of mortality.

This form of typhus has been variously named by different workers in different countries. In the table below the names are listed:—

Japan :	Tsutsugamushi fever ('tsutsu' = disease and 'mushi' = a mite). Japanese river fever. Flood fever. Kedani fever (Kedani = hairy mite).
Sumatra :	Pseudotyphoid. Mite fever.
Malaya :	Scrub typhus. Tropical typhus. Rural typhus. K form of tropical typhus.
Australia :	Mossman fever. Endemic glandular fever. Coastal fever. Endemic tropical typhus.
New Guinea :	Endemic typhus.
Indo-China :	Le typhus exanthematique. Pseudotyphus of Deli. 'Fievre fluviale d'Extreme Orient.' Tropical typhus.
India :	XK typhus. Mite typhus. Malayan scrub typhus. Tsutsugamushi fever.

Some workers have felt that since the clinical features of the disease in the different geographical areas show variations particularly with regard to the presence of eschar and the fatality rate, one name would not suit all types. At least four names have been suggested, *viz*, Tsutsugamushi fever, Pseudotyphoid, Mossman fever and Scrub typhus. The characters on which the division into types is based are presented in tabular form below:—

Country	Eschar	Case fatality rate
Japan	'Never lacking'	22 to 68 per cent.
Sumatra	'Always present' in Europeans. In natives less frequently, 40 per cent.	4 to 9 per cent in indigenous population.
Malaya	10 per cent Europeans, 2.5 per cent Asiatic labourers.	14 per cent in severe form.
Australia	'In many cases' eschar found.	Less than 1 per cent.
New Guinea	'Constant feature'	20 per cent.
Indo-China	'Frequently seen' in European cases.	14 per cent.
India	Not seen in 'natives'. 35 per cent in outsiders and severe cases. Nil in local inhabitants and mild cases.	Nil in 'natives'. 10 to 15 per cent in outsiders. Nil in local people and mild cases.

It will be seen from the table that the variations do not appear to be greater than what is generally observed in other diseases. Also, as far as the evidence goes, the causal agent, the nature of agglutinins present in the serum of patients and the mode of transmission in all these clinical types are very similar if not identical and as such it seems reasonable to consider them all as one disease. In that case the name tsutsugamushi has precedence over all others and should be adopted.

The causal agent of mite typhus is *Rickettsia orientalis*. The other names for it are *R. nipponica*, *R. tsutsugamushi* and *R. akamushi*. This organism can be grown in tissue culture and in the yolk sac of the developing chick embryo. A study of the various strains of this organism isolated in different countries has shown their close relationship if not absolute identity. All strains are comparatively less infective to guinea-pigs and more infective to white mice; they give rise usually to local necrotic lesions accompanied by fever on intradermal inoculation into monkeys; the serum of convalescent monkeys and guinea-pigs agglutinates proteus OXK antigen (but not OX19 antigen) in the same manner (though in a lower titre) as the sera of humans suffering from mite typhus do,

cross-immunity experiments also support the view that all strains are very closely related.

The epidemiology of the disease as studied in different countries bears a very close similarity. In Japan, the disease is confined to river valleys with sandy soil, generally overgrown with grass and scrub and subject to flooding. Labourers working in such areas contract the disease. In Sumatra, it is found in plantations where workmen are engaged in clearing land overgrown with bush and grass. The disease occurs here during the rainy months. In Malaya, it is a disease of the open scrub country where labourers work for one reason or another or soldiers are camped. In Australia, it occurs among workers in sugarcane plantations, among woodcutters in jungles and among labourers clearing scrub in areas situated near the sea coast having a damp sandy soil. In New Guinea, it occurs among people engaged in clearing virgin bush or in mining. Cases occur throughout the year and have no relationship to rainfall (Blake *et al.*, 1945). In Indo-China, it prevails during the rainy season in plantations located in river valleys subjected to flooding and among labourers engaged in woodcutting or brush and weed clearing.

The animal reservoir of infection is believed to be one or other species of rodents. In Japan, the field rodent *Microtus montebelli* has been shown to be naturally infected with *R. orientalis*. In Sumatra, the house rat *Mus concolor* and the field rat *Mus diardii* have been suspected. In other areas different species of wild rats and bandicoots have been shown to harbour *R. orientalis* infection in them (Lewthwaite and Savor, 1936; Cook, 1944).

As regards the arthropod vector, the Japanese workers produced evidence between 1907 and 1917 to show that *Trombicula akamushi* was the carrier of tsutsugamushi fever. They were successful in transmitting the disease to a few monkeys through field and laboratory experiments. But their work has never been confirmed. In the other areas of prevalence the mite *T. deliensis* is chiefly suspected. But up to the present no conclusive evidence of its rôle in transmission has been obtained. The disease has not been transmitted to experimental animals or to man by the bites of infected larval mites. In certain endemic areas where other species of mites abound, species other than *T. deliensis* have been suspected to be responsible for transmitting the disease.

If rodents are the reservoirs of infection and larval mites the transmitting agents, the mechanism of transmission based on the available knowledge of the life-cycle and bionomics of the mites would be as follows: Larval mites are parasites of rodents. They acquire infection by feeding on infected rodents. After engorgement with tissue juices of an infected rodent host, they drop off into the soil. The engorged larval mites do not feed again on a

vertebrate host. Hence they cannot transmit the infection to another host, themselves. The engorged mites complete their cycle of development into nymphs and adults in the soil. The nymphs and adults feed only on insect eggs and they are also therefore not responsible for transmission of infection to man or rodents. Eggs laid by infected adult mites give rise to infected larvæ, the infection being transmitted through the ova. These newly emerged infected larvæ attach themselves to rodents or men for a meal and during the act of feeding transmit the infection to their host.

Although this is the alleged mechanism of infection no conclusive proof has yet been obtained to substantiate it. The chief difficulty in the way of obtaining proof has been the inability to breed trombiculid mites in the laboratory in sufficient numbers for conducting transmission experiments.

Nagayo *et al.* (1917) were the first to attempt to rear *Trombicula akamushi* in the laboratory for transmission experiments. They fed nymphs and adults on melon, potatoes and other vegetables and claimed to have obtained one generation but not a second. Using their technique, other workers failed to obtain successful results. During World War II when typhus became a serious problem with the army fighting in the Far Eastern Front, Blake *et al.* tried to obtain proof of mite transmission. But their attempts to carry mites through a complete cycle of development in the laboratory were unsuccessful. Wharton and Carver (1946) in U.S.A. found insect eggs a satisfactory food for nymphs and adults. Using this food they reared *Neoschomgastia indica* in the laboratory. They, however, stated that 'no entirely satisfactory system for culturing trombiculid mites has yet been described'. Michener (1946) and Jenkins (1947) in U.S.A. reared nymphs and adults of certain American chigger mites using mosquito eggs as food. They claimed to have reared two generations. So far as *T. deliensis* is concerned, no one has successfully reared them in the laboratory. The position with regard to typhus transmission at the end of 1947. was that unless a technique was developed for rearing the suspected trombiculid mites in large numbers in the laboratory no solution of the transmission problem could be obtained.

Observations on the epidemiology of NK typhus in Barrackpore

Barrackpore is a small cantonment town situated 14 miles to the north of the city of Calcutta on the banks of the River Hooghly. It has a mixed military and civil population. The total population which was 25,395 in 1931 rose to 32,751 in 1941 and is now estimated at 40 thousand. The Ishapore Rifle Factory, the Calcutta Water Works, a large park, a race course and Government House are located there. There are many barracks and camps for troops

and there is also a small bazaar. Much cultivated and uncultivated land is found all around the town. Some of the land is covered with scrub or grass and some areas are swampy. The soil is alluvial and composed of sand, silt and clay. The months of heavy rainfall are June, July, August and September when about 10 to 12 inches of rainfall are recorded per month and the mean temperature varies from 80° to 90°F. Occasionally heavy downpours are recorded, raising the total monthly rainfall to 25 inches or more. November, December and January are the cold months when the mean rainfall is about 2 inches and temperature between 60° to 75°F. The humidity except during the cold weather is fairly high. The chief febrile diseases prevalent are malaria, kala-azar, enteric fever, typhus and dengue. There are a few hospitals to meet the needs of the civil and military population.

As regards the history of typhus in the province of Bengal in general and in Barrackpore in particular there are no records to show that typhus fevers were prevalent to any appreciable extent prior to 1940. Bradley and Smith (1912) recorded one case of suspected typhus in a British sailor in Barrackpore. Basu (1924) described 15 cases resembling typhus occurring in Calcutta. Boyd (1935) reported 92 cases among soldiers of whom some were alleged to have contracted the disease in Calcutta. These cases were serologically diagnosed and they belonged to all three types XK, X19 and X2. Between 1940 and 1943 the army authorities drew special attention to the occurrence of typhus fevers among troops stationed in several areas in the plains of Bengal (Calcutta, Barrackpore, Jhikargacha, Panagarh, etc.). On the basis of the Weil-Felix reaction these cases belonged to all three types XK, X19 and X2. In 1943-1944 an outbreak of typhus was reported from Darjeeling-Gloom area. Serological investigation of these cases showed that they belonged mainly to the X19 type. But whether they were of the flea-borne or louse-borne type was not conclusively established. In 1945, Lusk reported 54 cases diagnosed by the Weil-Felix test in an Indian military hospital in Calcutta and among these 42 were XK, 8 X19 and one X2. Roy (1946) reported 10 cases. These cases also belonged to the XK, X2 and X19 types. In the autumn of the same year an unusual increase in fever cases was reported among the civil population of Barrackpore. These cases were suspected by the local doctors to be paratyphoid on clinical grounds and we were asked to investigate the outbreak. Laboratory investigations soon revealed that about 20 per cent of the fever cases admitted into hospitals in the area at the time of the enquiry (during the months of October and November) were definitely typhus. Since then all three kinds of typhus have been shown to be prevalent in Barrackpore with XK typhus as the predominant type. Now cases of typhus are occurring regularly in the area

throughout the year, the maximum incidence being between May and October.

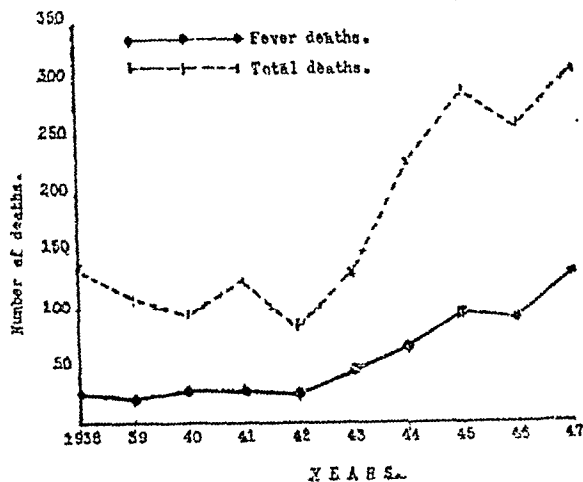
In order to determine whether typhus fever had been occurring in the Barrackpore area in an unrecognized form for a long time previously or whether it was a newly introduced disease, enquiries were made of the military and civil authorities. Enquiries of the military authorities brought out the following facts: that sporadic cases of typhus fever had been occurring since 1905 among the troops resident in the area; that with the stationing of increased numbers of troops during World War II the number of typhus cases increased; that cases occurred mostly in those who were stationed in camps and sheds built close to large open fields and on hitherto unoccupied land near the River Hooghly; that the incidence and severity of the disease among the new-comers were greater than among the old residents; that the investigation conducted by them did not support the view that the disease was introduced into the area by the troops although this possibility cannot be completely ignored; and that they believed that Barrackpore was an old endemic area but due to lack of proper laboratory facilities typhus was not diagnosed till recently among the civil population. Enquiries of the local practitioners and government medical men in charge of hospitals showed that fevers resembling typhus had been prevalent in the area for a considerable time; that these cases were being diagnosed as enteric on clinical grounds—those that lasted for 10 to 12 days being generally diagnosed as paratyphoid and those that lasted for longer periods and were more severe being diagnosed as typhoid; that laboratory aid was seldom sought for diagnosis of cases; that during and shortly after the monsoon months every year fever cases increase; that since the stationing of larger numbers of troops in the area the fever incidence among the civilians had greatly increased; and that in 1946 this fact was brought to the notice of the health authorities. Our own investigation of over 500 fever cases between 1946 and 1948 showed (i) that typhus fevers of the three serological types, *viz.* XK, X19 and X2, are occurring in the civilian population; (ii) that XK typhus is the predominating type; (iii) that the majority of cases are mild and can readily be mistaken for other fevers such as paratyphoid dengue and influenza; (iv) that diagnosis of these cases on clinical grounds alone is difficult; (v) that laboratory facilities are not available in the area for establishing a correct diagnosis; and (vi) that the adult local population suffer less than adult new-comers. From the evidence collected it seems justifiable to conclude that typhus fevers must have been occurring among civilians for many years past and that Barrackpore must really be considered as an old endemic area. It is hardly feasible that infected rats or trombiculids were carried by troops into the station. The military authorities who had better provision for

laboratory diagnosis of these diseases diagnosed the disease earlier than the civilian authorities and brought to light the prevalence of the disease among the troops as far back as 1905. With the stationing of large numbers of troops and the influx of refugees from all over the country into the area the incidence of typhus shot up both among the civil and military population.

In chart I the total deaths as well as deaths from fevers for the period 1938 to 1947 among the civilian population are shown.

CHART I

Chart showing total deaths & fever deaths in Barrackpore



It will be seen that deaths from fevers have gone up enormously in the area. The ratio of fever deaths to total deaths has increased from 1 : 6 in 1938 to 1 : 3 in 1947. While the death rate from fevers was only 70 per 100,000 in 1938, it had reached 320 per 100,000 in 1947. For want of accurate figures total fever cases treated in the hospitals are not shown. But enquiries have revealed that they have risen from a few hundreds to a few thousands (i.e. from about 400 to 3,000). Among these about 25 per cent are malaria, 10 per cent enteric, 5 per cent kala-azar, 10 per cent typhus and 50 per cent all other fevers. Out of 538 cases of fever admitted in the civil hospitals during our investigation between October 1946 and October 1948, 102 cases were diagnosed as typhus on the basis of clinical and laboratory findings. It would thus appear that typhus fevers are an important cause of morbidity in the area and their importance is as great as that of enteric fevers which are also prevalent there.

XK typhus occurs in the Barrackpore area in two forms, viz, mild and severe. 80 per cent of cases belong to the mild type and 20 per cent to the severe type. The case fatality in the mild type is nil while that in the severe type is 14 per cent. Mild cases are noticed mostly among the local people (children and adults) and the severe cases amongst the new-comers to the area (Indian and European adults).

The age incidence of the disease as noted in over 100 cases is given below :

1 to 5 years	.. Nil.
6 to 10 years	.. 8 per cent.
11 to 15 years	.. 10 " "
16 to 20 years	.. 16 " "
21 to 25 years	.. 16 " "
26 to 35 years	.. 21 " "
36 to 50 years	.. 23 " "
over 50 years	.. 6 " "

It will be seen from the table that the majority of cases occurred in adults. The youngest case was 7 years of age and the oldest 56 years.

As regards sex distribution, 19 per cent of cases occurred in females and 81 per cent in males.

The cases belonged in order of importance to the following occupation groups :

Factory labourers residing in camps; water works labourers residing in the fields adjoining the water works.

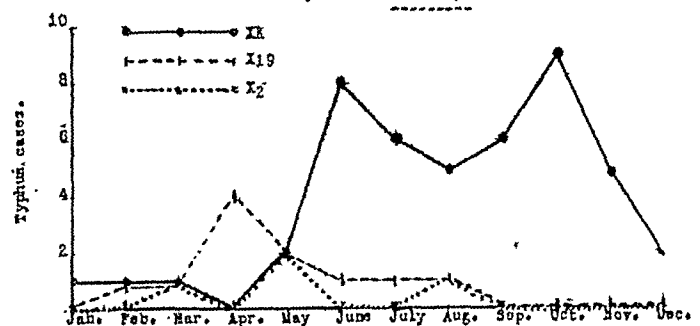
Police constables who are on patrol duty at night; *durwans* who guard cultivated lands, barracks, camps and water works.

Coolies who work in agricultural land and children residing in houses close to uncultivated waste land.

The season of maximum prevalence of typhus was the rainy season beginning in May and ending in November. A few cases occurred in the other months as well. Chart II gives the incidence of typhus per month for 1947 and 1948.

CHART II

Chart showing incidence of typhus cases by months in Barrackpore area.



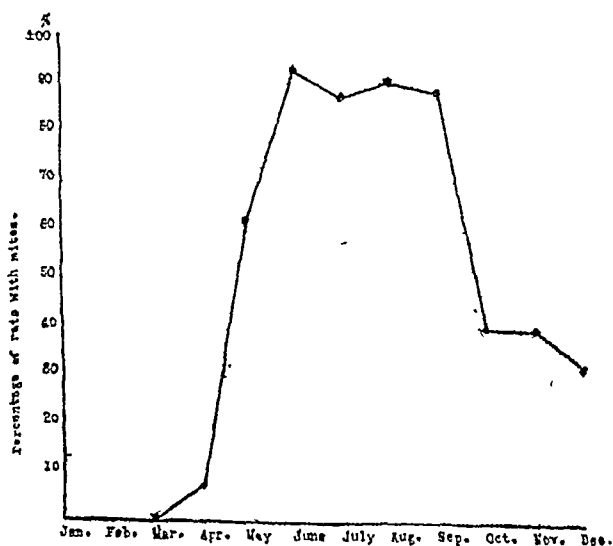
In 14 cases of XK typhus the presence of rickettsia in the blood was demonstrated by intraperitoneal inoculation of washed blood cells into white mice. White mice, which were first demonstrated by us in 1942 to be very susceptible to infection with *R. orientalis*, have been found to be the most suitable for experimentation with this rickettsia. All strains tested produce ascites and enlargement of spleen and death of the mice usually occurs in about 8 to 18 days. The Barrackpore strains are not very pathogenic to guinea-pigs. But after passage through mice, virulence seems to be somewhat increased and inoculation gives rise to fever about 8 to 10 days

later. If the animal is sacrificed slight ascites is found and also rickettsia can be demonstrated in peritoneal and tunica scrapings. If the animal is not sacrificed it almost invariably recovers and the serum of recovered guinea-pigs shows agglutinins for proteus OXK. In a few cases intradermal inoculation into monkeys—*Macacus rhesus*—was tried, but it did not result in the production of a necrotic ulcer. In one monkey a lump formed at the site of inoculation about the size of an almond. No rickettsia was found in the scrapings from this lump but the monkey showed a rise of temperature from which it recovered and its serum showed agglutinins for OXK. Also one* of the workers in the laboratory who accidentally inoculated his finger with rickettsia while injecting an experimental mouse developed an eschar of the papular type with lymphangitis and enlarged glands in about 10 days. This was followed by a severe attack of typhus from which he recovered. His blood showed agglutinins for OXK and rickettsia were demonstrated in animals inoculated with washed blood cells.

During the investigation 1,064 rats were trapped in the area. They belonged to 4 species: *R. rattus*—74 per cent, *Gunomys varius*—13 per cent, *Bandicoota indica*—1 per cent and *Cocidura coerlea*—12 per cent. 32 per cent of the rodents caught were found to harbour mites of one species or more and of the infested ones 72 per cent harboured *T. deliensis*. In rats caught between January and April the rate and intensity of infestation were small (2 to 10 mites per rat) but during the rainy months, May to November,

CHART III

Showing percentage of mite-infested rats with *T. deliensis*.



the rate and intensity of infestation were much higher (50 to 150 mites per rat), vide chart III. It was noticed that young rats were seldom infested. This suggests that mites do not

probably breed in nests of rats but that they get attached when the rats emerge for food or water. *Rattus rattus* and shrews were found most frequently and intensely infested with *T. deliensis*. In the others only mild infestations were seen and much less frequently. In shrews the site of election for *T. deliensis* was the outer side of the fore and hind legs, and the base of the tail; they were found less frequently in the ears. In *Rattus rattus* they were found in the ears mostly.

The larval mites found infesting rats were identified. They were found to belong to three genera—*Trombicula*, *Neoschongastia* and *Schongastiella*. Among the trombiculid mites in which our main interest lay several species were found. *T. deliensis*, *T. muris*, *T. munda*, *T. spicia* and two other new species not yet fully studied or named. Of the mites found the predominant species was *T. deliensis*. These were found most frequently in the rainy months which were also the months of maximum prevalence of typhus. Chart III shows the percentage of mite-infested rats showing *T. deliensis*.

A comparison of charts II and III will show the correlation between typhus incidence and prevalence of *T. deliensis*.

Having found that *R. rattus* is more heavily and frequently infested with *T. deliensis* than other rodents, an attempt was made to find out if any of the rats were infected with *R. orientalis*. Since we had found white mice very susceptible to infection with this rickettsia, these animals were inoculated intraperitoneally with 1 cc. of brain emulsion from rats showing heavy infestation with *T. deliensis*. This was done so as to ensure a greater degree of success in isolating the rickettsia. Out of 30 rats examined, 8 were found infected. These 8 strains were tested by mouse inoculation and 6 gave rise to pathological lesions identical with *R. orientalis*, i.e. produced ascites and enlarged spleen and also caused death of the mice in 8 to 18 days, average 12 days. These strains, when inoculated into guinea-pigs, behaved like rickettsial strains from human sources and caused fever for a day or two but no death. The serum of recovered guinea-pigs showed OXK agglutinins to a titre of 1 in 125. All these six strains have been provisionally accepted as *R. orientalis*. The other two were considered to be some other strains of rickettsia. From these observations it may be concluded that organisms identical with *R. orientalis* are found in about 20 per cent of *R. rattus* found heavily infested with *T. deliensis*.

In the course of our investigations several attempts were made to rear *T. deliensis* in the laboratory for use in transmission experiments but success was not achieved until we began to use *Culex* eggs as food for the nymphs and adults. Towards the end of 1947, a technique was developed by which successive generations of *T. deliensis* could be reared in the laboratory in large numbers without any difficulty. A

* This is the medical man commented upon by Chaudhuri and Chakravarti, on p. 48.—EDITOR, I.M.G.

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REFERENCE

LAL, R. B., and SEAL, General Health Survey, S. C. (1944). Singur Health Centre, Preliminary Report, Government of India Press.

The Indian Medical Gazette Fifty Years Ago

GEOLOGICAL STRATA AND PLAGUE

(From the *Indian Medical Gazette*, Vol. 34, p. 64)

MR. C. L. GREISBACH, Director of the Geological Survey of India, said in his evidence before the Plague Commission that from the list of localities it appeared that by far the largest number of plague cases had occurred on soil covering Deccan trap and crystalline rocks and only a very small number on the great alluvial belt stretching from the Indian Ocean to the Bay of Bengal. The former formation roughly coincided with the distribution of laterite deposits. The total number of cases was as follows between September 1896 and November 1898 :—

On trap and crystalline rocks ..	150,929
On the Indus-Ganges alluvium ..	12,936
GRAND TOTAL ..	163,865

Of this grand total the cases which had occurred on the Great Indian alluvium formed only 7.88 per cent. At first sight this appeared very striking and seemed to point to the trap and crystalline area as being specially adapted to the spread of the disease, but in reality there was a more probable explanation for these figures at hand. A look at the geological map of India would show that Bombay was situated near the centre of the western margin of the great Deccan trap plateau. When the exodus of the scared population began after the outbreak of the plague in 1896, the refugees naturally moved in all directions and spread themselves fanlike over the adjoining country, and this happening to be all composed of Deccan trap and beyond it of crystalline rocks, the overwhelming majority of cases on these formations seemed easily explained. It had been shown that so far at least it had not been conclusively proved that soils without the intervention of man spontaneously developed diseases. But, on the other hand, there were abundant evidences that the tenacity with which certain epidemics clung to localities were influenced by the geological formation on which they appeared. In Western India the soil was generally very thin and rested frequently direct on laterite deposits which were among the most

spongy and generally porous rocks known. In such cases it might well be that the direct sources of epidemic might sink some considerable depth into the underlying rock, but this would have to be proved. He accepted the general medical opinion that geological formations had nothing to do with the distribution of epidemics beyond the different physical characteristics attaching to various formations, some being porous and others less so.

Current Topics, Etc.

Intravenous 'Paludrine' (Proguanil)

By R. N. CHAUDHURI
and

H. CHAKRAVARTI

(Abstracted from the *British Medical Journal*, i, 15th January, p. 91)

PALUDRINE acetate (soluble proguanil) was tried intravenously as an experimental measure in a series of 11 cases of malaria, all of which except two had *P. falciparum* infection. The majority of the patients had either cerebral or gastro-intestinal complications and were not suitable for oral medication. Four of them were gravely ill.

Doses varied from 25 to 400 mg., and were repeated in a few cases. The total amount of paludrine injected ranged from 200 to 600 mg. per case.

This series was too small for determination of the optimum dose, but in the majority of cases a dosage of 200 to 400 mg. controlled the temperature and cleared the peripheral blood of asexual parasites in two to three days.

This was especially noticeable in case 4, that of a man of 60, who was semi-conscious and in a toxic state on admission. After receiving 400 mg. in twelve hours, he soon became fully conscious and began to take his food much better. Cases 8 and 10, which had oral paludrine in addition to injections, showed equally good response even before the drug by mouth could have exerted its full effect.

One patient admitted in a moribund state died. Another patient, with typical cerebral malaria, remained unconscious for several days and later developed signs and symptoms of encephalitis, from which, however, he recovered completely.

The injections were well tolerated, but one patient (and another not included in this series) had some phlebitis of the injected vein, which subsided in a few days.

Paludrine acetate has now been replaced by paludrine lactate, which is more soluble and less irritant. An ampoule of 2 ml. contains 100 mg. of the drug.

Heterospecific Pregnancy : I. The Clinical Importance of the Rh Factor

By P. M. DE BURGH *et al.*

(Abstracted from the *Medical Journal of Australia*, 5th February, 1947, Vol. 1, p. 174)

THE serological findings are correlated with the clinical histories of 54 mothers in whom Rh iso-immunization was suspected.

o important questions are raised; the first is whether an absence of evidence of iso-immunization adds the Rh factor in the aetiology, and the second is whether the finding of iso-immunization necessarily means that the Rh factor is involved.

The results recorded show that when evidence of iso-immunization against the Rh factor is obtained in an Rh-negative woman, the Rh-positive child causing the immunization was or will be affected by hæmolytic disease of the newborn. In this series there were two possible exceptions (cases 8 and 12) to this general statement.

However, the finding of iso-immunization in a patient during pregnancy is not necessarily a poor prognostic sign for the unborn child. If the father is heterozygous the foetus may be Rh-negative and unaffected, and the iso-immunization may be the result of a previous pregnancy or blood transfusion. This possibility must always be considered before the patient's confinement. Information is required on the changes which occur in the titre of the antibodies during pregnancy.

The results are less enlightening on the question whether hæmolytic disease of the newborn may be due to Rh incompatibility in the absence of evidence of iso-immunization revealed by present methods of testing. At first sight it would appear that the histories in cases 50 and 51 could be explained only on the basis of such an incompatibility.

It would appear that as a general rule the finding of evidence of iso-immunization in a pregnant or parturient woman is closely correlated with the finding of some degree of hæmolytic disease of the newborn in the child; but this correlation is not absolute. The examination of the mother's serum before confinement is, therefore, of great prognostic value. The examination of her serum after confinement has diagnostic value, because hæmolytic disease of the newborn rarely if ever occurs in the absence of positive serological findings.

Rubber versus Antibiotics

(Abstracted from the *Lancet*, i, 25th January, 1947, p 147)

THE experiments of (Cowan, S. T., *Lancet*, i, 1945, 178) two years ago showed that up to 50 per cent of antibiotic activity may be lost during the passage of aqueous solutions of penicillin through the rubber tubing of a continuous drip-apparatus.

All materials—rubber, glass, or metal—that are to come to contact with antibiotics should clearly be tested for any inactivating effect.

American workers (Huelsenbeck, J. B., Foter, M. J., Gibby, I. W., *Science*, Vol. 104, 1946, 479) have found that 4 of 11 samples of synthetic rubber and 1 of 5 samples of natural rubber completely destroyed penicillin in solution within 24 hours.

The inactivating effect of rubber varies widely in different samples and is not correlated with the colour of the tubing.

As a rule glass has hardly any action on penicillin, but cheap soda glass may give off enough alkali to raise the pH and reduce the stability of penicillin solutions.

The simple tests in testing a sample rubber vary from one in which an inch of tubing is placed in 10 ml of penicillin solution in a screw-capped bottle—this assumes that the glass is inert—to one in which 3-foot length of tubing are filled with solution, after contact for some hours the solutions are re-assayed and the percentage loss in activity is determined.

Preliminary tests indicate that neither natural nor synthetic rubber has any deleterious effect on solutions of streptomycin.

The Practical Application of DDT for Malaria Control in Rural and Urban Areas in India

By I. M. PURI

(Abstracted from the *Indian Journal of Malariology*, 1, 1947, p 211)

THE property of DDT, which has proved most important in the control of mosquitoes and other noxious insects, is its residual toxicity to those which come to rest on surfaces on which it has been applied. It is a slow-acting insecticide and has no apparent immediate action on the mosquito coming into contact with it. If, however, the insect has been exposed to the minimum lethal dose, it will die in four to six hours. The mosquito can acquire this minimum lethal dose merely by resting for a sufficiently long period on a surface on which DDT has been sprayed. The length of contact necessary to produce the lethal effect varies directly with the period which has elapsed since the time of application, and up to a certain limit inversely with the amount of DDT deposited on the surface. The results of experiments carried out in different parts of India and in other countries show that the duration of the residual toxicity of DDT sprayed on a given surface varies in different localities, the effective periods recorded varying from eight to ten weeks up to four or five months, or even longer. As the acquisition of the lethal dose of the insecticide depends on the length of contact, the effectiveness of the residual toxicity in any area is naturally influenced by the resting habits of the mosquitoes.

Experiments have shown that for indoor spraying a dosage of 50 mg. of DDT per square foot will keep down the number of mosquitoes appreciably for over eight weeks, and if properly sprayed on the walls, one, or possibly two, applications at this dosage are enough for a short malaria season of three to four months. It may be mentioned that if only the walls and ceilings of occupied houses are treated, a number of safe resting places are provided for the mosquitoes by clothing, saddlery, untreated furniture, freshly spun cobwebs, etc., in the rooms. This will naturally tend to counteract the residual effect of the DDT deposits in the houses. When applying DDT, all possible surfaces should be thoroughly and carefully sprayed, even though such treatment considerably prolongs the actual spraying time.

COMPOSITION OF DDT SPRAYS

DDT may be applied in the form of a solution, emulsion or suspension. Although DDT-kerosene oil solution has proved satisfactory, the pronounced smell which lingers for two or more days after treatment and the temporary hazard of fire, especially in bamboo and thatched huts in rural areas, are both serious disadvantages. For these and other reasons, the superiority of emulsions and suspensions over solutions is now widely recognized. A 12.5 to 25 per cent emulsion or suspension should be used at the rate of 4 to 2 cc per square foot on a wall surface with the help of a stirrup pump the output of which is 450 cc. per minute.

A number of methods for the preparation of suspensions have been tried at the Malaria Institute of India. The commercial DDT obtainable in India at the present time is extremely coarse, and has to be thoroughly ground to render the particles small enough to disperse uniformly in water. Consequently, wet grinding of the coarse DDT available was tried in the presence of a wetting agent which would also facilitate grinding. Among the various adjuvants used, gum acacia and gelatine were found to be the most effective, and with their help a paste containing 55 to 60 per cent DDT can be easily prepared. For the preparation of this concentrate, no elaborate apparatus is necessary and 1 lb of DDT may be ground into a thin paste in half an hour in an ordinary stone mortar (diameter

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10 inches X depth 5 inches) with a stone pestle. The ingredients necessary for the preparation of the suspensions are readily available in any bazaar in India. The three alternative formulæ which were found to yield the best results are given as follows, in order of merit:—

- (1) DDT 605 gm., gelatine 10 gm., water 485 cc.
- (2) DDT 605 gm., gelatine 5 gm., gum acacia 10 gm., water 480 cc.
- (3) DDT 605 gm., gum acacia 25 gm., water 470 cc.

EQUIPMENT FOR APPLICATION

A stirrup pump is the most satisfactory and economical apparatus for applying DDT as an indoor residual spray under Indian conditions. Although it is a two-man unit, it is very mobile and less fatiguing to use than knapsack sprayers. It is advisable to pass the spray through muslin, so as to remove any extraneous matter which would otherwise block the nozzle.

COST OF TREATMENT

An analysis of the various experiments carried out at Delhi and Quetta has shown that a dosage of 50 mg. of DDT per square foot, if sprayed in the form of a suspension, keeps down the density of mosquitoes very considerably for ten weeks or more. Even smaller dosage of about 35 mg. of DDT per square foot or 1 cc. of 25 per cent DDT spray per square foot applied twice in three months is probably sufficient in bringing about a marked fall in the incidence of malaria.

In a rural area with a short malaria season necessitating only a single application of DDT, the expense of malaria control with DDT residual spray works out at 7.9 annas per hut and the expenditure *per capita* will be about 2.0 annas calculating at the rate of 4 persons per hut. With a somewhat longer season (about 20 weeks) the second application need be of only half the dosage (25 mg.) of DDT per square foot, and the total cost for two applications under such circumstances works out at 13.95 annas per hut, the expense *per capita* being 3.49 annas.

The Use of Curare in Abdominal Surgery

By V. O. McCORMICK

(Abstracted from the *Irish Journal of Medical Science*, November 1947, p. 681)

THE two preparations which are now in common use are the original intocostin introduced by Squibb and the d-tubocurarine chloride, subsequently prepared by Burroughs Wellcome, which has received the trade name of Tubarine, and it is to that preparation that all my personal remarks apply.

It must be clearly understood that the object of using curare in anaesthesia is to achieve muscular relaxation or to abolish a troublesome reflex. It has no power to abolish painful sensations, hence some form of anaesthesia must be used with this object in view. It is quite clear, however, that if only sufficient anaesthetic to abolish painful sensation need be used, and if muscular relaxation and the control of troublesome reflex action can be achieved by the addition of a non-toxic and rapidly eliminated drug, the total load which the patient will have to bear will have been considerably lightened.

We have now dealt with a sufficient number of cases to have formed the opinion that curare is a most valuable addition to our resources. The relaxation which it produces gives the greatest possible help in operating with the minimum amount of trauma and the necessity to use only the mildest and least toxic forms of general anaesthesia leaves patients in the best possible condition at the end of operation. Observations on blood pressure which we have made support the view put forward that the strain of operation and especially of loss of blood are much less harmful using

light anaesthesia, such as is possible with curare, than it is with the deeper anaesthesia necessary to provide muscular relaxation.

The relaxation which follows the administration of curare does not spare the muscles of respiration; the intercostal muscles are paralysed by doses which leave the diaphragm almost intact. It is absolutely essential that anyone proposing to use curare should be fully alive to the danger of depressed or arrested respiration and should be properly equipped to combat it by performing controlled artificial respiration. Patients should be connected to a closed circuit anaesthetic machine whereby respiration can be maintained by rhythmical compression of the bag; proper oxygenation is thus maintained and carbon dioxide at the same time prevented from accumulating in the system. With ordinary doses respiratory depression sufficient to need artificial respiration frequently does not occur at all, but should it occur, it does not usually last more than three or four minutes and need not cause the slightest anxiety. Owing to the muscular relaxation and absence of reflex irritability the artificial respiration is invariably easy to perform.

At first we were haunted by the fear of operating on a patient who, while able to feel the pain of the operation was yet unable owing to the paralysis to show any sign of suffering by movement of hand or face. Except in the case of extreme susceptibility to the drug, or of the use of doses greatly in excess of what we now employ, I do not think this could occur. I have seen patients who exhibited good abdominal relaxation and yet were able to make reflex movements of hand or face when still lightly anaesthetized. Should an operation be persisted in while anaesthesia has become too light, shock may develop and it is important that a watch should be kept on the pulse rate, as a rise in pulse rate is sometimes the first sign that the depth of general anaesthesia needs to be increased. Nevertheless, it is not at all uncommon to be able to perform an extensive upper abdominal operation under a moderate dose of pentothal, followed by gas and oxygen for the rest of the operation. It is important to realize that some of the more potent drugs, such as ether, appear to have a reinforcing effect on the curare action and doses of curare should be less when it is intended to use such drugs subsequently.

Our custom has been to start off with a modest dose, use it as long as it was effective and then to administer further smaller doses as necessary. We have noted that although the full effect passes off quite rapidly (20 to 30 minutes) there must be a considerable persistence of effect, because a small increment will reproduce the original condition of full relaxation. A final dose should not be given shortly before the patient is due to leave the theatre. Under no circumstances should any patient whose respiration is depressed be allowed out of the immediate control of the anaesthetist. Details of the technique we have adopted and the cases in which it has been employed are to be given and I would like to stress the enormous advantages it offers for certain types of cases. First, the debilitated patient whose only chance is a severe, difficult and often prolonged operation. To be able to give first-class operating conditions without heavy doses of toxic drugs is an enormous help. Secondly, in any case in which even moderate muscular relaxation is required in a 'tough' subject. We are all familiar with these people and the nightmare they are to anaesthetists. With curare to provide relaxation and pentothal and gas and oxygen or cyclopropane to provide sleep, things both during and after operations are very much happier than heretofore.

TECHNIQUE

Our practice, which has now become standardized, has been to start with an initial dose of tubarine. A small quantity of blood is then aspirated into the syringe to wash the tubarine out of the needle and the pentothal syringe is then attached to the same needle and pentothal administered as necessary. As

soon as the patient is asleep we insert a pharyngeal airway and attach the patient to the anaesthetic machine, which is set to give a weak nitrous oxide mixture. The operation then proceeds and, if muscular relaxation is inadequate, further small doses of tubarine are given from time to time. As a rule when one gramme of pentothal has been given a further deepening of anaesthesia is obtained by increasing the strength of the anaesthetic mixture or, if this is not sufficient, by substituting cyclopropane for nitrous oxide. We do not care to use ether or trilene, and would not consider using chloroform.

COMPLICATIONS

Complications occurring during operation have been few. Respiratory depression occurred in almost all cases. Complete respiratory arrest was encountered in a small number. Whenever respiration was small in volume it was supplemented by squeezing the bag to improve ventilation. The respiratory depression lasted for a variable time—from 3 to 15 minutes—and was never a cause of anxiety. It should be remembered that this depression is due to the combined effect of curare and pentothal. In only one case did we find it necessary to give prostigmine.

In two cases unusual cardiac irregularities developed. Both these cases were partial gastrectomies, induced with kemithal and the irregularity developed when the patients were curarized, and gas and oxygen was being administered. The irregularity took the form of a sudden halving of the pulse rate. In one of these cases we succeeded in obtaining an electrocardiograph, which showed the irregularity to be due to extrasystoles. The pulse returned to normal in each case after about 20 minutes.

DOSAGE

We adopted 15 milligrammes as the standard initial dose of tubarine and only occasionally departed from this. Subsequent doses were given, they were deemed necessary and our custom was to give either 10 or 7.5 milligrammes for the second dose. A third dose, if necessary, was usually not more than 7.5 milligrammes. The duration of the curare effect varies considerably. In some cases a second dose was needed after 15 or 20 minutes, whilst in others satisfactory relaxation would last for 45 minutes. Resistance to the drug varies considerably. The largest dose in any one case was 45 milligrammes, the smallest 7.5 milligrammes.

RESULTS

One hundred and fifty abdominal cases that have been given curare are reported. There were no deaths during operation. Ten patients died following operation. These deaths do not appear to have any bearing on the advantages or disadvantages of curare in anaesthesia.

The most striking feature of these patients is their good condition both during and following operation. The clinical impressions are borne out by readings of pulse and blood pressure taken at regular intervals, which frequently show no significant change through the course of a prolonged and difficult operation.

Isotopes in Blood Circulation

(From *Science and Culture*, Vol. 13, September 1947, p. 109)

RADIO-ACTIVE iron and iodine have made possible a study of shock and have provided new knowledge about blood circulation. Red blood cells were tagged with two kinds of iron and blood serum albumin tagged with radio-active iodine. Report from works at Harvard Medical School reveals that regardless of cause during shock red blood cells get trapped in the tiny blood vessels in all organs of the body. Evidently

treatment of shock should be devoted not only to restoring the total volume of blood in the body but also towards starting the blood flowing again in the capillary blood vessels. The present method of studying blood circulation is by the use of a blue dye and by centrifuging a sample of blood and measuring the mass of red cells collected at the bottom of the tube. Persons who had hæmorrhages showed discrepancies in the results by the above methods.

Evaluation of Penicillin in the Treatment of Yaws

By J. H. DWINELLE *et al.*

(Abstracted from the *American Journal of Tropical Medicine*, Vol. 27, September 1947, p. 633)

An analysis of the results of treatment of 500 cases of primary and secondary yaws infections with penicillin, in aqueous solution and in oil with beeswax, is presented. Follow-up clinical and serologic observations were made on 446 of these patients for varying lengths of time up to 12 months. Three hundred and twenty (71.7 per cent) were followed for a period of 10 to 12 months after treatment.

Clinical response to treatment was uniformly excellent but serologic response was not. Only 16.6 per cent of the 446 patients were considered to show 'apparent cure'. An additional 75.1 per cent showed 'satisfactory progress', totalling 91.7 per cent. The remaining 8.3 per cent of the patients showed 'unsatisfactory progress'. In the latter group were included cases of 'reinfection', 'clinical relapse', and 'serologic relapse'.

The per cent of 'apparent cures' was higher, 26.7, in the group of hospitalized patients treated over a four-day period with penicillin in aqueous solution than in the two groups treated with penicillin in oil with beeswax on an ambulatory basis over two days, 11.0, and one day 6.4. However, there was a correspondingly higher proportion of cases showing 'satisfactory progress' in the latter two groups of patients so that when one combines cases of 'apparent cure' with those showing 'satisfactory progress' the total per cent is almost identical in the three groups of patients, 90.2, 92.9, and 92.8, respectively.

It is appreciated that follow-up observations over a period of 10 to 12 months after treatment are not sufficient to permit a comprehensive evaluation of the efficacy of penicillin in the treatment of yaws. Also, it is not possible to make a strict comparison of the results of treatment of penicillin in aqueous solution with penicillin in oil with beeswax, because of the difference in treatment schedules employed. However, it is felt that penicillin is probably the present-day drug of choice in the treatment of yaws, and that penicillin in oil with beeswax is of considerable public health value in countries such as Haiti where large numbers of patients must be treated on an ambulatory basis in rural clinics. Its use can be expected to successfully control cutaneous lesions and therefore prevent the spread of infection.

Surgical Glove Powder

(From the *Medical Journal of Australia*, Vol. 2, 18th October, 1947, p. 477)

Various workers have, from time to time, drawn attention to harmful effects believed to be due to talc used on surgical gloves. The facts are, however, not widely known or appreciated, and it seems desirable to draw attention to two recent reports on the subject. C. B. S. Roberts, assistant to the professor of pathology in the University of Glasgow, has discussed the pathological findings in seven cases of silicious granuloma all

occurring sometime after laparotomy. In two cases the lesion developed in the scar in the abdominal wall (an appendectomy scar in each case) and in five cases granuloma developed in the Fallopian tubes. The scar lesions were moderately painful; the tube granulomata created the clinical effect of a low-grade pelvic inflammation and caused sterility. Silicious particles found in the lesions resembled in size and shape the spicules of talc used by surgeons for dusting gloves. The pathological nature of the lesions is considered to be much the same as that of traumatic silicious granuloma; the mode of arrival of the silica in the area is the contentious point, but there seems little reason to doubt Roberts's conclusion that it was deposited from the surgeons' gloves at the time of operation in the form of talc (talc is a naturally occurring magnesium silicate). The important consideration, as Roberts points out, is that prophylaxis is essential; it does not seem likely that the occlusion of the Fallopian tube can be remedied once it has occurred. A substitute for talc is needed.

Some careful experimental work on various glove powders has been carried out in the United States by C. Marshall Lee and Edwin P. Lehman, of the University of Virginia School of Medicine. Their main concern was with the production of adhesions by talc and comparison of its effect with other powders suitable for use as a substitute. A standard operation was performed on a series of dogs, and the same quantity of each of a series of otherwise suitable dusting powders was scattered as evenly as possible over the bowel and mesenteric surfaces of a respective animal. The quantity was the maximum amount (determined by experiment) which could be expected to be deposited by an operating team of four persons. The powders used were talc, tantalum oxide and three specially prepared corn starch derivatives. All were satisfactory from the point of view of their physical properties, their capacity to be sterilized and their stability under the conditions necessary to their use. The results were striking. In a control animal operated on without the introduction of any powder, no adhesions formed. The introduction of talc produced dense generalized adhesions, a result that was also obtained later with much smaller amounts of talc; macroscopic and microscopic examination revealed the close association of the talc with the adhesions. Tantalum oxide produced equally extensive adhesions. Two of the corn starch derivatives produced a small number of adhesions, and one was completely absorbed from the peritoneal cavity without the production of any local ill-effects whatever; the latter result was confirmed repeatedly. Moreover this non-irritating powder (known as 'Starch No. 108' and prepared by a well-known firm) was superior to talc in its flow and dusting qualities, both in the raw condition and after having been autoclaved. Experiments have so far revealed no sensitizing or anaphylactogenic properties of the powder, though this is the subject of further investigations.

In both of these discussions the use of talc is strongly condemned and the grounds of criticism appear sound. It is not known whether 'Starch No. 108' as used by Lee and Lehman is commercially available, but it seems clear that the continued use of dry gloves dusted with talc cannot be justified.

Experience with Pteroylglutamic (Synthetic Folic) Acid in the Treatment of Pernicious Anæmia

By B. E. HALL

and

C. H. WATKINS

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. 32, June 1947, p. 622)

FOURTEEN patients who had Addisonian pernicious anæmia in relapse were treated with pteroylglutamic

(synthetic folic) acid over periods from twenty-four days to nine months. The most striking effect of this form of therapy was observed in the bone marrow, erythropoiesis rapidly changing from a megaloblastic to a normoblastic type. However, considerable variation in the rate of erythrocytic regeneration was encountered, and in certain instances normal blood values were not obtained after several months of treatment with pteroylglutamic acid in doses generally thought to be relatively large.

Symptomatic improvement also was variable. Treatment resulted in abatement of glossitis and peripheral neuropathy in most cases, but recurrence was common among persons maintained solely on this form of therapy for a period of months. Moreover, peripheral neuropathy and subacute combined degeneration of the spinal cord developed as new manifestations in a significant proportion of cases two to five months after treatment was begun. In the light of these observations it is obvious that pteroylglutamic acid does not prevent the occurrence of degenerative disease of the peripheral nerves and spinal cord in pernicious anæmia and that the use of this form of therapy as a substitute for extracts of liver or gastric mucosa subjects patients to the hazards of progression or development of the neural manifestations of the disease. On the other hand, pteroylglutamic acid has been found to be an effective therapeutic agent in certain macrocytic anæmias related to pernicious anæmia, a subject not considered in the present paper.

The Toxic Effects of Ten Daily Injections of Mapharside Combined with Penicillin in the Treatment of Early Syphilis

By R. R. WILCOX

(Abstracted from the *Journal of the Royal Army Medical Corps*, Vol. 89, August 1947, p. 49)

THE toxic effects of a schedule consisting of 600 mg. of mapharside given in ten daily injections combined with 2.4 million units of commercial penicillin have been described.

In all nearly 1350 cases were treated and there was 1 fatality. In addition there were 2 severe, 1 mild and 1 doubtful case of arsenical encephalopathy. No immediate case of jaundice occurred in the entire series.

Four hundred and five of the cases treated at one hospital have been studied in greater detail.

Treatment was modified in 72 of which 30 were due to an excessive fall in the white cell count; 24 to a secondary pyrexia associated in 3 with 1 severe, 1 mild and 1 doubtful case of encephalopathy, in 2 with nine-day erythema, and 2 with other symptoms. Treatment was adjusted in 7 others for skin complications, 5 on account of headaches and in 6 others for a variety of symptoms.

There was no case of jaundice though 19 had transient urobilinogen in the urine and treatment was not modified. The incidence of Herxheimer reactions was not affected according to the duration of the disease though secondary cases generally required the treatment to be modified more frequently than those of primary syphilis.

Asepsis in Spinal Anæsthesia

(From the *British Medical Journal*, i, 10th May, 1947, p. 647)

SINCE the earliest days of spinal anæsthesia a small proportion of patients given spinal anæsthetics have subsequently developed a type of meningitis which we discussed in these columns earlier this year. In a number a recently reported case in which meningitis has

followed a spinal anæsthetic the nature of the infection has not been such as to suggest the skin, either of the patient or of the operator, as its source. It has been due, almost without exception, to some sort of Gram-negative bacillus, either *Ps. pyocyanea* or a non-descript organism of the type commonly found in non-sterile water. Moreover, non-sterile water has been incriminated as its source, the needle and syringe used having been 'dished up' in supposedly sterile water which was subsequently suspected or proved not to have been sterile. The clearest proof of this origin was obtained in the Sheffield series of cases described by Barrie; 11 out of 96 patients given spinal anæsthetics in one operating theatre developed meningitis, and the source of infection was found to be a defective Berkefeld filter supplying supposedly sterile water. A similar source was suspected in the two fatal cases of *Ps. pyocyanea* meningitis described by Evans. Suggestive evidence of his possibility was furnished by the finding of the same organism in the cerebro-spinal fluid of another patient without meningitis, this contamination being traced to a Winchester quart bottle of 'sterile' distilled water. A bottle of sterile distilled water or saline cannot be depended on to remain sterile if it has once been opened.

A further series of cases due to the same type of infection, but of undiscovered origin, was recently described in this *Journal* by Vuylsteke. Evans, in a further publication, and Garrod, who has recently reviewed this problem, make suggestions for a sterilization technique whereby such accidents can be avoided. Everything used for lumbar puncture, whether for spinal anæsthesia or for any other purpose, should be adequately sterilized by heat. Boiling will serve if necessary; dry heat is much to be preferred, and has the advantage that it can be applied at leisure, the apparatus then being always available for use when required. What should be avoided at all costs is some sort of chemical treatment, often itself unreliable, such as storage in spirit, and 'dishing up' in water alleged to be sterile. This seemingly innocent liquid, harmless enough if introduced into any other part of the body, is fraught with danger.

Recommendation as a Medicine

(Abstracted from the *British Medical Journal*, ii, 19th July, 1947, p. 114)

By the Pharmacy and Medicines Act, 1941, if a person sells by retail any article recommended as a medicine, the article or its container must be labelled with the appropriate designation and quantities of its ingredients. A 'substance recommended as a medicine' may only be sold by a doctor, a dentist, an authorized seller of poisons, or a person who has served a regular apprenticeship to a registered pharmacist.

Messrs. Potter and Clarke, manufacturing chemists, asked the opinion of the High Court in a friendly action against the Pharmaceutical Society on whether a specified series of common laxatives with specified labels were 'substances recommended as a medicine'. The label on senna pods merely gave that name and the name and address of the firm. Their cascara was labelled 'Trade Mark: Winged Lion Brand. Fluid Extract of Cascara Sagrada. British Pharmacopœia. Dose, half to one teaspoonful in half a wineglass of water'. Lemon and squil linctus was merely labelled with its name and the name and address of the firm. Compound rhubarb pills also bore the name and the dose. 'Effervescent Powders' was labelled 'Extra Strong Effervescent Powders. Prepared by Carter and Sons, Sheffield, a wartime substitute for Seidlitz Powders, Carters', with instructions for use and the manufacturer's address. The firm maintained that these medicines, so labelled, were not 'substances recommended as a medicine' and so could lawfully be sold by unqualified persons. Mr. Justice Wynn-Parry

held that they were right in regard to the senna pods and the linctus but not in regard to the other substances, presumably because the dosage was specified.

The firm appealed, arguing that the written terms must specify the particular ailment or groups of ailments for the prevention or treatment of which the substance is appropriate. The Pharmaceutical Society argued that this was not necessary if it was common knowledge that the substance was in fact used for the prevention or treatment of a specific ailment or group of ailments. For example, the label on the cascara, though it did not mention constipation, might be nevertheless calculated to lead to the use of fluid extract of cascara sagrada for the prevention or the treatment of constipation. The same, they said, applied to the rhubarb pills and the seidlitz powder substitute: both were well-known household remedies.

The Court of Appeal held that the relevant words of the Act were neither doubtful nor ambiguous. They did not think that Parliament would have desired to make the criminal liability of a seller of medicine depend on the accuracy of his speculation concerning the exact extent to which the general knows that a particular medicine is a remedy for a particular ailment. If the written terms contain only an accurate description of the substance it is not 'recommended'. To render it 'recommended' its description must indicate that it is a remedy for a specified ailment. They therefore held that the three laxatives in question could, with the given labels, be sold by unqualified persons.

Tolerance of Man Towards Hot Atmospheres

By E. F. ADOLPH

(Abstracted from the *Supplement No. 192 to the Public Health Reports*, 1946)

1. A PRACTICAL limit to tolerance for heat is signalled by the premonition of collapse (heat exhaustion) experienced by acclimatized men. The collapse represents an inadequate circulation of the blood, with or without high bodily temperatures.

2. At temperatures below this practical limit, considerable physiological strain and discomfort prevail. They indicate definite disadvantages for human activities. No amount of morale can compensate for the physiological strains imposed by a hot atmosphere.

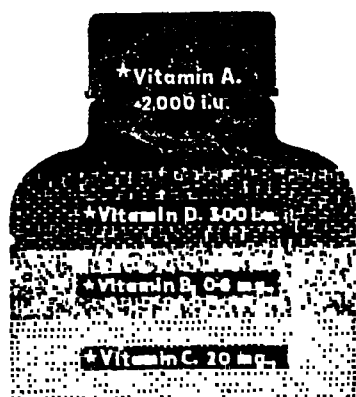
3. The wet-bulb temperature is a useful index to intolerable conditions. Temperatures above 90°F. can rarely be endured indefinitely. During work the intolerable temperatures may be as low as 80°F. or less.

4. The effective temperatures (sensibly equivalent temperatures) are an accurate index of physiological stress, in so far as those temperatures have been determined at particular physical activities and in scant clothing.

5. Initial acclimatization is in the majority of persons nearly complete after four exposures of two hours each to limiting temperatures. There is suggestion of additional slower acclimatization requiring a month or more.

6. The variability in heat tolerances among individuals is reduced by their acclimatization. The range of the remaining variability is still vast, and may at present be put to advantage only by assay of individuals at the assigned tasks.

7. Factors that help men to endure high temperatures are: shade, breeze sufficient to keep the skin dry, no clothing if already shaded, acclimatization to heat, plenty of water and salt, physical fitness, and adequate sleep. Factors known to threaten endurance are radiation, heavy or impermeable clothing, heavy work, alcohol, diarrhoea or vomiting, lack of appetite for food, and wounds or infections.



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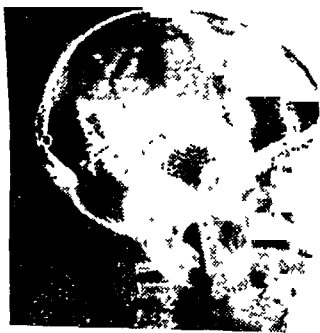
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Above: Figure 1.

Below: Figure 2.

R. J., age 49. Motor cycle accident. Admitted in deep coma, with large scalp wound and contusion over right temporal and parietal region.

X-Ray showed multiple linear fractures with large depressed fragments, plus fracture of right zygoma and fractures of the base of the skull (Fig. 1).

Operation: Toilet of the scalp wound, removal of large area of depressed bone which had penetrated the cortex in an area of 2-in. diameter. Cortical debris removed, together with fragments of bone. Temporal facial graft sutured over dural gap. Scalp wound closed (Fig. 2). Skull cap of Gypsona P.O.P. applied (Fig. 3).

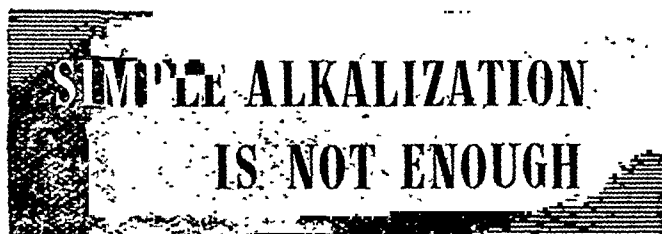
Feeding by indwelling naso-pharyngeal catheter carried out during period of semi-coma.



These details and illustrations are of an actual case. T. J. Smith and Nephew, Ltd., of Hull, England, manufacturers of Gypsona P.O.P. and Elastoplast bandages, publish this instance—typical of many—in which their products have been used with success.

Figure 3.





It is true that excess of gastric acidity may be neutralized by the simple administration of bicarbonate of soda; but this measure produces only a transitory effect

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Bacteriophage Under the Ordinary Microscope

By A. W. HOFFER

(Abstracted from the *Journal of Bacteriology*, Vol. 53, June 1947, p. 781)

EXPERIMENTS were begun (1) to find whether the small particles present in bacteriophage preparations and shown by the electron microscope could be stained and made visible under the ordinary microscope, and (2) to learn, if possible, whether these particles are, indeed, bacteriophage. These particles have a diameter greater than that of bacterial flagella.

Bacteria for inoculating peas and bacteriophages specific for these bacteria were used in these investigations.

Three staining methods, each having its own advantages and disadvantages, were developed for demonstrating these particles under the ordinary microscope: (1) staining with carbol auramin and examining under ultra-violet irradiation, (2) a modification of the Ziehl-Nielsen acid-fast stain, and (3) a modification of the Hofer and Wilson flagella stain.

It has been shown that the particles in question are ordinarily acid-fast.

By staining preparations of various ages, it became apparent that the particles enlarge in size in the presence of bacteria; that they increase in number as the bacterial cells decrease; and that the particles developing in the partially lysed cells and showing in the zones where bacterial cells have been before lysis has occurred stain particularly sharply.

Using the newly developed phase microscope, it has proved possible to see the same particles unstained while they are still in living condition. In this way, it is possible to see and to photograph the successive stages of lysis; the immobilization of the cells; the appearance of the larger, i.e. visible, bacteriophage particles; union of these with the cells; the preliminary diminishing of the size of the granules subsequent to attachment to the cells; and, immediately following, the increase in size of the former at the expense of the cells, until the latter burst and the protoplasm flows out. Finally, there is development within the cell protoplasm of new bodies similar to the original granules. These observations seem to demonstrate that the particles under observation actually are those of bacteriophage.

Furthermore, after observing under the phage microscope the various stages of lysis, it was possible to re-examine under the ordinary microscope preparations made by the acid-fast technique and to locate therein structures that have previously been seen only under the phase microscope. This demonstrates both the existence of the bacteriophage particles and the usefulness of the ordinary microscope for seeing them.

A Feeding Experiment on Indian Army Pioneer Recruits, with Special Reference to the Relative Value of Meat and Milk in Rations

By O. P. VERMA *et al.*

(Abstracted from the *Indian Journal of Medical Research*, 35, April 1947, p. 41)

THE analysis of the data reported in this paper indicate that when 12 ounces of fresh mutton (meat diet) or 48 ounces of fresh milk (milk diet) or 2 ounces of fresh mutton plus 1½ ounces of tinned fish plus 2 ounces of skimmed milk powder (basic diet) are added to an otherwise constant diet conforming to a generally satisfactory nutritional standard, meat diet produces a weight gain which is significantly greater than that produced by the milk diet or the basic diet in subjects

showing deficiency signs. On the other hand, we have the impression on purely clinical evidence that the milk alone caused a relatively greater improvement in skin texture.

The effect of meat on the weight gains of our subjects was somewhat unexpected. It is not due to a greater caloric intake on the part of the meat group, and, therefore, seems to be due to some nutritional quality inherent in meat. In the absence of definite evidence, we can only speculate on the nature of this nutritional quality. It is generally accepted that the proteins of milk have exceptionally good growth-promoting qualities (as would be expected in a foodstuff which forms the sole source of nourishment for new-born animals). While we have not attempted to review the literature in detail, there does not seem to be any conclusive evidence that the proteins of meat possess growth-promoting qualities superior to those of milk. (It should be remembered that in all the diets under consideration, an ample supply of protein and a high proportion of animal protein—for Indian diets—was available.) It is possible that the effect of meat was not due to protein but to a stimulating effect on metabolism generally.

The present finding that meat has a value superior to that of milk for promoting increase of weight, together with that of Hynes *et al.* that meat has special value in blood regeneration, requires careful consideration and, if possible, experimental confirmation, in connection with nutritional policy in India. It is believed that this is the first experimental evidence derived from work on human beings, that a lacto-vegetarian or semi-vegetarian dietary may be intrinsically inferior to a meat dietary. The implications in respect of a predominantly vegetarian population like that of India do not require stressing.

Thomson *et al.* have stressed the value of really nutritious diet in the physical regeneration of under-nourished Indians recruited into the army. The work now reported confirms this view. The South Indian recruits dealt with are among the smallest and most ill-nourished recruits which the army has ever accepted. With proper feeding and a healthy environment, they can be and are being transformed into reasonably useful soldiers who can undertake the strenuous work required for pioneers. The physical disabilities imposed on them by continued under- and malnutrition during childhood and adolescence can by no means be overcome entirely by good feeding when normal growth has practically ceased; but if better recruits are not available, it pays to provide the best diet that can be provided. According to our findings, meat should form a substantial part of such a diet. In the case of South Indian recruits, there is no difficulty in persuading them to eat 12 ounces of meat daily, and this would probably be true of all classes except those whose religion imposes a definite ban on the consumption of meat. This is stressed, since it is often stated that the majority of Indians would not eat meat even if it were provided.

'The Vile Weed'

(From the *New York State Journal of Medicine*, Vol. 47, 15th March, 1947, p. 608)

THOSE persons who insist on smoking that 'vile weed', tobacco, will see the error of their ways after reading the following words of James the First of England, quoted in a *Treatise on Tobacco, Tea, Coffee, and Chocolate* by Simon Pauli, London, 1746, in the Library's collection.

'At least, therefore, O Citizens, if you have any Sense of Shame, or Dread of Infamy, left in your Bosoms, lay aside the *Use of Tobacco*, a Custom attended with Ignominy, received through Error, and established by Stupidity. By its Means the Wrath of Heaven is excited against us, the Health of our Bodies

impaired, our Substance wasted, and the Dignity of our Nation not only diminished at Home, but also despised Abroad; for Tobacco is a substance loathsome to the Sight, disagreeable to the Lungs, and, by its Clouds of black smook, nearly resembling the horrid Steams of Hell.'

Bubonic Plague in East Prussia

(Abstracted from the *Medical Press*, Vol. 218, 23rd July, 1947, p. 95)

A REPORT has been received that epidemic bubonic plague has inflicted an extremely serious mortality amongst the civilian population during June 1947.

Anti-N and Other Low-Temperature Agglutinins in Human Serum

By E. N. ALLOTT
and
C. A. HOLMAN

(Abstracted from the *Lancet*, ii, 26th July, 1947, p. 130)

SEVERAL abnormal agglutinins acting at low temperatures, including one anti-N and three anti-P agglutinins, have been met with. These are regarded as of natural, rather than immune, origin.

Though the agglutinins did not act at 37°C., agglutination took place in tubes which had been incubated at 37°C. and subsequently allowed to stand on the bench before microscopical examination.

It is necessary to be on guard against such atypical agglutinins when testing for Rh antibodies. Any laboratory undertaking serious Rh-testing must have a panel of available donors whose MN and P characters are known besides their ABO and Rh groups.

Treatment of Disseminated Sclerosis

(Abstracted from the *Lancet*, ii, 26th July, 1947, p. 143)

In his Humphrey Rolleston lectures at the Royal College of Physicians last week Professor P. C. P. Cloake mapped out pitfalls in the treatment of the disease. Despite his caution there seems to be real promise that the treatment which he has practised for the last 17 years is an advance on existing alternatives. Broadly, it is based on repeated courses of T.A.B. pyrotherapy along with alternating courses of intravenous organic arsenic and oral inorganic arsenic. These remedies, as Professor Cloake said, have been used before in disseminated sclerosis; the novelty lies in this insistence that their administration must be continued for at least five if not ten years.

Out of 422 cases observed, 312 have been followed up. Of 64 slight cases that received adequate treatment, 39 are to-day well, 20 are improved, and 5 are unchanged; none is worse. Among the moderately severe cases, only 1 is materially worse. It is all too easy, as Professor Cloake indicated, to draw over optimistic conclusions from these results; for example, the patient who felt that he was not benefiting from treatment may not have stayed the course; and will thus have been lost to the follow-up. This does not alter the central fact that for all their deficiencies the figures seem better than those obtainable with other forms of treatment.

Plea for a Study of Social Aspects in Leprosy

By P. SEN, M.B.

(From *Leprosy in India*, Vol. 19, October 1947, p. 123)

DR. SEN in this article makes a *prima facie* case for institution of a study in sociology in leprosy. He says

that for successful control of leprosy doctors should consider the character and personality of each patient, know his environment and take into account all the social and emotional factors that may disturb him. The basis of any programme must be a broad concept which includes both organic and social components of the disease, and not organic component alone. The social problems of the patient have been defined and evaluated on the basis of a combination of medical and social data. He then describes the various principles and methods of such a study.

Staining of Spirochaetes for Microscopic Examination

By S. VAGO

(Abstracted from *Trop. Dis. Bull.*, Vol. 44, No. 8, August 1947, p. 755)

A SIMPLE and rapid method is described for the staining of spirochaetal organisms. It is claimed to be suitable for all types of spirochaetes including those that are difficult to stain. The procedure is as follows:—

1. A thin and uniform smear is made on a clean slide and dried in air;
2. it is first stained with a concentrated aqueous solution of mercurochrome and then rapidly washed in water (to remove excess of stains);
3. it is finally stained with a concentrated aqueous solution of pytonin (methyl violet) and washed in water. The film is dried and it is ready for examination. The spirochaetes stain blue-black.

It is claimed that this method is not only applicable to those species which are readily stained but also certain pathogenic species which are notoriously difficult to stain, e.g. *Tr. pallidum*, various species of leptospiræ, etc.

Practical advantages: (1) Preliminary fixation and heating unnecessary. (2) Time of staining less (actual time for staining not mentioned). (3) Shape of the organisms and their coils preserved. (4) Preparation of the staining solutions easy, no weighing is necessary. (5) The staining solutions keep indefinitely without deterioration. (6) No heating of the staining solutions is required.

S. S.

Reviews

OBSTETRICS AND GYNÆCOLOGY: A SYNOPTIC GUIDE TO TREATMENT.—By Beatrice M. Willmott Dobble, M.A., M.B., F.R.C.S., D.M.R.E. 1948. H. K. Lewis and Co., Ltd., London. Pp. xi plus 358 with 22 illustrations. Price, 20s.

As the name of the book indicates and as the author mentions in the self-explanatory preface, this work is not a textbook. It is essentially a handbook of treatment for the practitioner. It deals with all essential matters in everyday obstetrics and gynæcology that come in the way of a general practitioner in whose clientele there is a considerable number of women.

From a practical point of view the section on obstetrics in the discussion of labour there are two good chapters, one on domiciliary midwifery, normal, and the other on domiciliary midwifery, abnormal. These chapters contain a wealth of details of great use to a practitioner fresh from the protective surroundings of an up-to-date hospital or a training centre.



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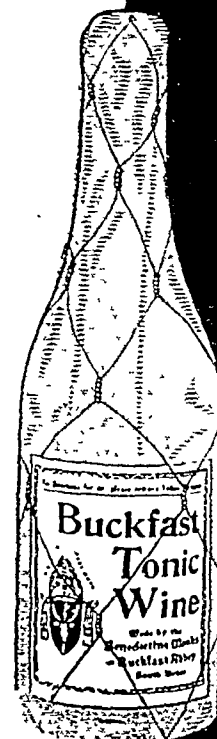
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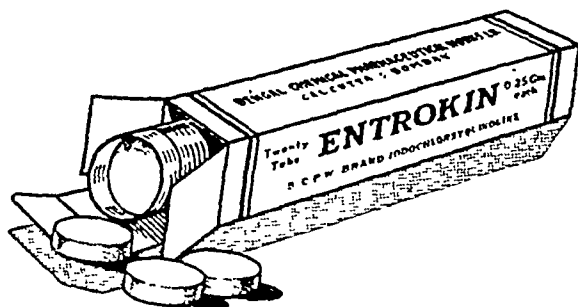


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The method of discussions and the general trend of style in the whole book is of a mediocre type. The author says in the preface: 'It is to the general practitioner, above all, that these pages are addressed and especially to the novice . . .'. This being the author's objective, critical discussions of vexed subjects and questions of treatment would have been out of place. In fact, even though there is a chapter on the rhesus factor in obstetrics, nothing theoretical or of academic interest has been discussed. There are some very valuable practical hints and lessons for the young practitioner. Chapters XX, XXI and XXII in obstetrics and XL and XLI in gynaecology are very good.

The author has adopted the didactic tone throughout the text. It is not possible to agree with whatever he says. Some of his ideas do not fall in with what is expected as standard and universal. Here are some examples:—

- Page 26. 'It may be necessary to douche the uterus repeatedly during the operation (evacuation of hydatidiform mole) . . .'
- " 28. Curettage of the uterus has been advocated to establish the diagnosis of tubal gestation. We think this a very dangerous diagnostic procedure. The author says 'A dead tubal pregnancy (tubal mole) *usually* is absorbed'. We definitely object to the word italicized.
- " 87. The author recommends that the newborn baby's mouth should be cleansed *before* the eyes are swabbed. The author has put 'before' in italics. We are, however, so very anxious to prevent ophthalmia neonatorum that we give preference to the swabbing.
- " 146. The author says the legs are almost always extended in primipara. Everybody does not share the author's experience. We do not agree in adopting the routine procedure of drawing off the liquor amnii in hydramnios as recommended by the author on page 160.

The printing and the general get-up of the book are excellent.

M. N. S.

BACTERIAL AND VIRUS DISEASES.—By H. J. Parish, M.D., F.R.C.P.E. 1948. E. and S. Livingstone Ltd., Edinburgh. Pp. 168. Illustrated. Price, 7s. 6d. Postage, 6d. (home)

THIS little book written by a practical immunologist presents in a very convenient form the essential principles of immunology and their application to medicine. Students and practitioners will save much time in obtaining the latest information on testing, immunizing actively and protecting passively a subject at risk. The author for this purpose has separated the essential from the non-essential admirably.

The sections dealing with diphtheria and tuberculosis deserve special notice. The former gives all that has reduced the incidence of and mortality from diphtheria in Great Britain within recent years. The latter gives all that is being practised globally to-day and is about to be undertaken on a large scale in India.

The last word is available on all sera and vaccines, and on their preparation and application. Even history of immunology has been included, complete with photographs of Jenner, Lister, Pasteur, Behring, Ehrlich and Paik.

Suggestions for further reading are also available for advanced workers.

The printing is remarkably free from flaws of the first edition. On page 33 an error has been blacked out, a suggestion to authors who do not like errata in their books.

S. D. S. G.

Correspondence

SKIN-GRAFTING

SIR,—What would be the consequences if two individuals were 'grafted' on to each other by means of a surgical operation? For instance, if small areas of skin on the back of the forearms were removed from the right of one and the left of the other and the raw areas approximated and stitched all round and both limbs immobilized in plaster of paris for a week. Would the operated area heal by first intention? If so, would the anastomosis between the two systems lead to any disastrous results in either or both individuals in the event of their being of different blood groups? Or would anastomosis or union not take place at all in such an event? Would anastomosis and union, then, take place between individuals of similar blood groups? Further, could such a measure, if it be possible, be of any therapeutic value in the treatment of anæmias or other blood diseases such as agranulocytosis or myeloid leukaemia?

Are there any instances of such experiments having been carried out and, if so, is there any literature on the subject? If not, I am sure this would be an interesting field for research and experiment, provided the 'anæmias' were forthcoming.

Yours faithfully,
S. A. A. SAMI,
Civil Assistant Surgeon.

BHAGALPUR.

HYDROXY STILBAMIDINE IN THE TREATMENT OF KALA-AZAR

SIR,—Hydroxy stilbamidine, or 4 : 4'-diamidino 2-hydroxy stilbene di-isothionate, is one of the aromatic diamidine compounds synthesized by Dr. A. J. Ewins, R.R.S. During the last four months, I have treated six cases of kala-azar with this drug at the School of Tropical Medicine, Calcutta. All the patients were admitted into the hospital of the School and the diagnosis was confirmed by finding the parasite, in spleen, sternum or tibia puncture smear. The patients were all Indians and of ages varying between 10 and 45 years. Five of the cases were previously untreated cases, and one a particularly stibio-resistant case. The total dosage was approximately 3 gm. per 100 lb. body weight in most of the cases, and this was spread out in about 20 doses. One patient had ten injections only and the total dose for him was 1.39 gm. per 100 lb. body weight. The drug was administered by the intramuscular route in some of the cases and by the intravenous route in the others. The intramuscular injections were painful but the intravenous injections given at a slow rate were well tolerated. Immediate clinical cure could be achieved in all the above cases. Further clinical trials of the drug are in progress and a fuller account of the results will be published when the investigations are completed.

Yours faithfully,
P. C. SEN GUPTA,
Officer-in-charge, Kala-azar Research
Department, School of Tropical
Medicine, Calcutta.

Dated the *5th March, 1949.

* Published in this delayed issue for February 1949.—
EDITOR, I.M.G.

Any Questions

TREATMENT OF ECLAMPSIA

SIR,—I was delighted to read the review by M. N. S. of Joseph Lee and Greenhill's 'Principles and Practice of Obstetrics', ninth edition, 1947, in your issue of August 1948, p. 395.

Your reviewer writes: 'We do not however accept all the lines of treatment recommended. We have disappointing results from the use of magnesium sulphate in eclampsia. We do not use hydrostatic bags in placenta prævia at all, nor do we teach our students to deliver the aftercoming head in breech presentation by application of traction with finger or fingers in the mouths'.

I shall feel extremely grateful if your reviewer kindly sees his way to giving the details of his methods of treatment in the three complications cited by him.

Yours faithfully,

HARIRAM MOHANDAS, M.B., B.S.

ANJAR (CUTCH).

[The main principles of treatment of eclampsia are: (1) to administer sedatives for the control and prevention of fits, and (2) to eliminate metabolic toxins through the bowel and the bladder. Intramuscular administration of magnesium sulphate in 12½ per cent or 15 per cent solutions is one of the methods adopted to produce a sedative effect. The following are the other methods: (1) Paraldehyde in olive oil, per rectum. (2) Chloral hydrate in water, per rectum. (3) Barbiturates, viz, sodium amytal . . . sodium, hypodermically. Morphine is the drug to be used freely, even one grain in 24 hours in quarter-grain doses each. The dosage of the other drugs to be used will depend upon the age of the patient, number and intensity of fits, presence of oedema, urinary findings and stage of labour, etc.]

Hydrostatic bags in placenta prævia are made of India rubber. This material perishes easily in tropical climates. The bags are often found to leak when wanted in an emergency. Placenta prævia is always an emergency. Moreover, the introduction of the bag is not feasible unless the internal os easily admits two fingers. The bag is therefore useless in all cases of complete placenta prævia and in many cases of incomplete placenta prævia. Moreover, the bag may be expelled suddenly, producing huge, even fatal, hæmorrhage. When the cervix is two fingers dilated and the cephalic end of the child presents, the membrane may be ruptured and traction applied on the scalp. This will effectively check the bleeding. If the podalic end is presenting a leg may be pulled down. In hospitals and institutions the best treatment under suitable conditions is of course Cæsarean section.

Traction in the jaw to deliver the aftercoming head is not only dangerous but is not wanted. If the head has entered the pelvic cavity, it is already flexed and the so-called 'Prague method' of delivery is usually sufficient. Where the head is above the pelvic cavity, shoulder traction, jaw flexion with supra-pubic pressure by an assistant is needed. Once the flexion is adequate, forceps application to the aftercoming head is very often helpful. It is understood that ideally all breech delivery should be conducted when the patient is under a general anaesthetic.—M. N. S.]

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL A. Y. DABHOLKAR, M.C., I.M.S. (Retired), was appointed as Officer on Special Duty in the Ministry of States, with headquarters at Poona, with effect from the 24th May, 1948.

The undermentioned I.M.S./I.A.M.C. Officers who have been released from the army service on the dates shown against their names are granted honorary ranks, as shown in the brackets against their names on release:—

INDIAN LAND MEDICAL SERVICE
SECONDED TO THE MEDICAL CORPS
(Emergency Commissions)

T./Major W. A. Nandedkar. Dated 19th December, 1946.

Captain S. C. Ghosh (Captain). Dated 15th September, 1947.

Captain V. L. Rao (Captain). Dated 8th July, 1946.

The undermentioned A.I.R.O. (M.) Officers relegated to reserve on release from mobilized service, on the dates shown against their names, are granted the honorary ranks of Major:—

ARMY IN INDIA RESERVE OF OFFICERS (MEDICAL)
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

Major Kundan Lal Malhotra. Dated 1st May, 1947.

Major Chandu Lal Malhotra. Dated 5th January, 1947.

LEAVE

Dr. A. G. Brooks, Officiating Assistant Director, Central Research Institute, Kasauli, was granted leave on average pay for 1 month with effect from the 15th December, 1948.

Publishers' Notice

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

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nor methyl testosterone sublingually appears to have any value in the treatment of angina pectoris'.

Selection of cases.—All anginal patients, reporting for treatment at the clinic, could not be considered suitable subjects for controlled observation and study.

Care was exercised, in the selection of patients for this study, to see: (1) That the diagnosis of angina pectoris had been clearly and firmly established on clinical and other grounds. Cases were admitted for study on the basis of the pain being typical with respect to site, radiation, onset, duration and response to rest and nitrites. (2) That the patients had already received some form of treatment or other, for some time past, without improvement, thus eliminating the likelihood of a 'psychic factor' from contact with the physician.

In this connection, cases of long duration are preferable for study because in such cases the diagnosis is certain, chances of getting spontaneous remissions are scarce and the patient is less likely to be influenced by the personality of the attending physician.

Preparation and dosage employed.—The preparation of testosterone propionate employed throughout the present investigation was Perandren (Ciba) in injectable and oily form.

In the great majority of our cases, 25 mg. of Perandren was injected intramuscularly, twice weekly, for a total period of six to eight weeks. However, in some of the cases, Perandren was injected thrice weekly for longer periods of time.

Criteria of improvement.—If during treatment with testosterone propionate, the anginal patient shows definite subjective improvement (e.g. diminishing frequency or absence of attacks, diminution in the intensity of individual attacks, increased capacity for walking or exercise, etc.) and if this improvement is confirmed by objective evidences (such as walking or climbing of longer distances without provocation of pain, definite reduction in the daily requirement of trinitrin tablets, exercise tolerance tests, electrocardiographic evidences of improvement, etc.), such evidence was taken as indicative of improvement.

Results have been classified, in accordance with Lesser's criteria, as 'marked improvement', 'moderate improvement' and 'no improvement' or 'failures'.

Grouping of cases.—One hundred and fifty cases of 'proved' angina pectoris were selected for the present investigation. Of these, 125 were reserved for testosterone therapy, the remaining 25 (*viz.* the 'control group') being treated differently. The cases were divided into the following three groups:—

Group I (labelled the 'primary' anginal group) was comprised of 85 patients having typical angina pectoris but with no history of previous coronary occlusion or thrombosis (even on close questioning). Of the 85 patients, 69

were males and 16 females, the youngest being 31 years of age and the oldest 88 years, the average age for the whole group being 56 years.

Group II (labelled the 'secondary' or 'post-thrombotic' anginal group) was comprised of 40 patients with typical anginal symptoms but with an irrefutable positive history or electrocardiographic evidence of previous coronary occlusion. Of the 40 cases in this group, 30 were males and 10 females, the youngest being 39 years of age and the oldest 83 years, the average age for this group being 51 years (*i.e.* 5 years less than the average for group I).

Group III (labelled the 'control' group) was comprised of 25 patients with typical angina pectoris (six of whom gave a history of previous coronary occlusion) who received (instead of testosterone) bi-weekly injection of an innocuous oily preparation (*viz.* 1 cc. camphro-salyl). The patients were kept in ignorance about the exact nature of the substance injected. Of these 25 patients, 21 were males and 4 females, ranging in age from 38 years to 67 years, with an average age of 54 years.

Groups I and II jointly represent the whole anginal group treated with testosterone propionate, the total number of patients so treated being 125.

Results of investigation

Part I: Expression of results in terms of improvement (according to Lesser's criteria)

According to Lesser's criteria (1946) a patient was classified as showing 'marked improvement' when he or she was able to increase his or her physical activity 'without precipitating an anginal attack for a period of at least two months' after cessation of testosterone therapy. Reduction in the number of attacks to less than half was classed as 'moderate improvement' whilst lack of appreciable reduction in the number of attacks after therapy was classed as 'no improvement' or 'failure'. Adopting these criteria of Lesser's the writer has been able to tabulate his results in table I.

Of 85 cases of 'primary' angina pectoris in group I, marked improvement was noted in 25.8 per cent, moderate improvement in 48.4 per cent and no improvement in 25.8 per cent. Out of every four patients in group I, one displayed marked improvement and two moderate improvement. The response to testosterone therapy, although satisfactory in both the sexes, was somewhat better in males (improvement being noted in 76.8 per cent of males and 62.4 per cent of females) (*see* table I).

Of 40 cases of 'secondary' or 'post-thrombotic' angina pectoris in group II marked improvement was noted in 50 per cent, moderate improvement in 27.5 per cent and no improvement in 22.5 per cent. Although the percentage of 'improved' patients was about the same in groups I and II of the series (*viz.* 74.2 per cent

TABLE I

Summary of results obtained with testosterone therapy in cases of angina pectoris
(for details please refer to text)

Group	Sex	Total number of cases	MARKED IMPROVEMENT		MODERATE IMPROVEMENT		NO IMPROVEMENT	
			Number	Percentage	Number	Percentage	Number	Percentage
All cases on testosterone (groups I and II).	Both	125	42	33.6	52	41.6	31	24.8
	Males	99	35	35.4	42	42.4	22	22.2
	Females	26	7	27.0	10	38.4	9	34.6
Group I. 'Primary anginal group'.	Both	85	22	25.8	41	48.4	22	25.8
	Males	69	19	27.5	34	49.3	16	23.2
	Females	16	3	18.8	7	43.6	6	37.6
Group II. 'Secondary anginal group'.	Both	40	20	50.0	11	27.5	9	22.5
	Males	30	16	53.3	8	26.7	6	20.0
	Females	10	4	40.0	3	30.0	3	30.0
Group III. 'Control group'.	Both	25	2	8.0	2	8.0	21	84.0
	Males	21	2	9.5	1	4.8	18	85.7
	Females	4	1	25.0	3	75.0

and 77.5 per cent respectively), 'marked improvement' was noted much more often in group II (i.e. the post-thrombotic group) than in group I (viz, 50 per cent and 25.8 per cent respectively) (see table I). Improvement was noted in 80 per cent of males and 70 per cent of females in group II.

When groups I and II of the series are considered jointly (i.e. 125 cases of angina pectoris treated with testosterone propionate injections), the results of this therapy work out as follows: Of the 125 patients so treated, 33.6 per cent showed marked improvement, 41.6 per cent moderate improvement and 24.8 per cent no improvement. In other words, taking all cases of angina treated with testosterone, only one of every 4 cases failed to show some degree or other of improvement. The percentage of 'failures' was somewhat higher in females than in males (viz, 22.2 in males and 34.6 per cent in females).

It is interesting to note that in the control group or group III 84 per cent of the cases failed to show subjective improvement of any sort.

Part II: Expression of results in terms of individual symptoms or features

This has been fully worked out in table II for 125 cases of angina pectoris treated with injections of testosterone propionate.

It will be noted that in 3 out of every 4 cases treated with testosterone, there was a reduction in the frequency of paroxysms, a diminution in the intensity of individual paroxysms and an increased capacity for effort. Temporary abolition of attacks was noted in one-third of the cases (33.6 per cent). In 4 out of every 5 cases treated, there was a general 'sense of well-being'

or subjective improvement after testosterone therapy (80.8 per cent).

TABLE II

Improvement in anginal cases after testosterone therapy (an analysis of individual features)

Feature analysed	Number of cases studied	Number improved	Percentage of success
1. Complete (temporary) cessation of attacks.	125	42	33.6
2. Reduced frequency of attacks 'to below half'.	125	94	75.2
3. Shortened duration of attacks.	78	44	56.4
4. Diminished intensity of attacks.	62	48	77.4
5. Increased capacity for effort.	25	19	76.0
6. General improvement (sense of 'well-being').	125	101	80.8
7. Reduced consumption of trinitrin tablets.	40	35 (?)	87.5 (?)
8. Exercise tolerance test (of Master and Oppenheimer).	5	3	60.0
9. Orthodiographic reduction in size of heart.	15	1	6.6
10. Electrocardiographic improvement.	20	2	10.0
11. Waldman's E.C.G. sign	9	2	22.2

Regarding the daily requirement of trinitrin tablets by the patient of angina the writer has found this test, in spite of being subject to errors of interpretation and to diurnal variations, a fairly useful index of the degree of improvement in these cases. Many of the cases have been trained to keep a daily record of the number of tablets required in order to 'keep themselves comfortable'. The results of this particular

investigation were indeed striking in some of the cases. For instance, in a Sikh patient (male), aged 56 years, the daily requirement of trinitrin tablets (gr. 1/100 each) dropped from 60 to 70 tablets to about 25 to 30, or less than half! Several of the patients were saved the necessity of taking a single tablet of trinitrin for several weeks or months after a course of testosterone propionate injections.

Routine electrocardiograms were taken before, during and after testosterone therapy (under standardized conditions) in about 20 of our cases of 'primary' angina. Cases of post-thrombotic or 'secondary' angina were considered unsuitable for this particular investigation, in view of the normal or spontaneous tendency to electrocardiographic improvement in these cases (in keeping with the natural processes of 'healing' of the myocardial infarct). Out of the 20 cases of primary angina thus investigated incontrovertible proof of electrocardiographic improvement was noted in only two. In one of these, there was definite improvement in the voltage of the T-waves in Leads II and III whilst in the other there was a definite reduction in the depression of S-T segments in Leads I, II and IVR together with an improvement in the voltage of T-waves in Leads I and IVR.

Waldman (1945) has recently reported that depression of S-T segments, so common in anginal cases after exercise tolerance tests, becomes less marked after testosterone therapy. The writer has been able to confirm Waldman's observation, to the satisfaction of his colleagues, in two of his cases.

Part III: A statistical analysis of all cases of angina pectoris treated with testosterone

The results of the analysis are incorporated in the accompanying table III.

Taking into consideration all the cases of angina pectoris, treated with testosterone reported in the literature up to date (and including the present series), the total number of cases works out at 376 cases.

Of these, improvement (marked or moderate) was reported in as many as 302 cases, i.e. in 80.3 per cent of the cases. The rest (i.e. 74 cases or 19.7 per cent) were regarded as 'failures'.

The analysis of the reported results of testosterone therapy in anginal cases shows that out of every 5 cases so treated, subjective improvement was noted in 4. In view of this satisfactory result, a more extensive application of testosterone therapy is urged in cases of angina pectoris.

Part IV: Further results of investigation

The onset of improvement.—According to Lesser, when improvement is noted after testosterone therapy, its onset 'varies with the individual both in time of onset and in degree'. The action of testosterone is 'not instantaneous' but is 'only slowly discernible'. Clinical improvement, when noted, is a matter of days or weeks.

In the present series of cases, improvement was noted most often after the fourth or fifth injection of testosterone although in 2 cases it was reported within a week of commencement of the therapy. In some of the cases, improvement was not admitted by the patient until after completion of the whole course of injections. In view of the delayed benefit in some of the cases, it is necessary to follow the case up for at least a month after cessation of testosterone therapy before labelling the case as 'not improved'.

Duration of relief.—According to Lesser (1946), the relief after testosterone therapy is

TABLE III

Results of testosterone propionate therapy in angina pectoris cases

(A statistical analysis of 376 cases reported in the literature up to date, incorporating the present series of 125 cases)

Author's name	Year of publication	Number of cases treated	Number improved	Number of failures	Percentage improved	Percentage of failures
1. Walker, T. C.	1940	5	4	1	80.0	20.0
2. Lesser, M. A.	1942	24	24	..	100.0	..
3. Hamm, L.	1942	7	7	..	100.0	..
4. Walker, T. C.	1942	9	7	2	77.8	22.2
5. Lesser, M. A.	1943	22	22	..	100.0	..
6. Sigler, L. H., and Tulgan, J. ..	1943	20	16	4	80.0	20.0
7. Levine, S. A., and Likoff, W. B.	1943	19	8	11	42.1	57.9
8. Strong, G. F., and Wallace, A. W.	1944	14	12	2	85.7	14.3
9. Waldman, S.	1945	10	7	3	70.0	30.0
10. Lesser, M. A.	1946	100	91	9	91.0	9.0
11. Levine, E. B., and Sellers, A. L.	1946	21	10	11	47.6	52.4
12. Vakil, R. J.	1948	125	94	31	75.2	24.8
All cases reported up to date (including the present series).	1940 to 1948	376	302	74	80.3	19.7

persistent, ranging from 2 to 34 months after cessation of treatment. In the present series of cases, the results have been on the whole less satisfactory. In the majority of successful cases, improvement was maintained, after treatment, for a period of one to four months, although in one case there was marked subjective improvement for as long as 7 months after cessation of therapy.

On the other hand, in some of the cases the therapeutic benefit was maintained only as long as the injections were kept up. After the injections were discontinued the anginal attacks returned to their original intensity and frequency within a few days or weeks.

Toxic reactions or untoward effects.—These were singularly few in the series of 125 cases. On only a few occasions were mild untoward effects noted, which could definitely be put down to administration of the therapeutic agent.

In the writer's experience the most common side-reaction was a 'sudden pain in one or more joints', lasting for several days and noted soon after the start of treatment in susceptible subjects. This arthralgic condition was particularly frequent in gouty and rheumatic subjects. Gouty subjects, who have been free of acute arthralgic attacks even for years, may develop a fresh attack of gout soon after the initiation of testosterone therapy.

The second commonest manifestation or side-effect noted was some form or other of vasomotor disturbance or imbalance; this may take the form of excessive flushing of the face with local 'heat', excessive sweating of the head and extremities, tingling or hyperæsthesia of the hands and feet, etc.

Next in frequency came palpitation, excess of 'libido', diarrhoea, giddiness or vertigo, nausea and vomiting, increase of peripheral oedema, low fever and spermatorrhoea, in that order.

Apart from these side-effects, encountered infrequently, testosterone propionate was very well tolerated in the present series of cases and appeared non-toxic even in doses exceeding the usual therapeutic doses.

Contra-indications to testosterone therapy.—On the basis of this experience, the following groups of cases seem rather unsuitable for testosterone therapy: (1) Subjects of gout, or rheumatism. In such patients, attacks of acute gout or arthralgia are likely to be precipitated by injections of testosterone (occasionally by the very first dose). (2) Subjects of diarrhoea. In such patients, the diarrhoea may be aggravated specially when testosterone is administered by the oral route. (3) Subjects of migrainous headaches, who have described an exacerbation of headaches after testosterone therapy. (4) Subjects who are 'over-sexed'. (5) Subjects of severe functional palpitation or vasomotor disturbances.

In any case, the above-mentioned objections to the use of testosterone are relative only and

the preparation may be tolerated quite well even in subjects displaying these disorders.

Tolerance of patients to massive doses.—Of the 6 patients of angina, who were given 25 mg. doses of testosterone propionate daily for 7 days (i.e. 175 mg. in a week) by Lesser (1946), two improved, two became worse, one remained unaffected and one developed acute pulmonary congestion with peripheral oedema.

In the writer's experience, even large doses of testosterone propionate are well tolerated by these patients. Out of 8 patients, who received daily injections of 25 mg. for 8 days (i.e. 200 mg. in 8 days) 3 showed subjective improvement, 3 displayed minor reactions (viz, flushing, palpitation, arthralgia and diarrhoea) and one developed oedema of both legs.

The anginal pains decreased in 3 of these 8 cases, became worse in 3 and remained unaffected in 2. Two patients have been able to tolerate a total dosage of 400 mg. of testosterone propionate (injectable) a month, for over 6 months, with no apparent ill-effects except an increased libido.

Correct dosage of testosterone propionate.—Although no hard and fast rules can be laid down for the ideal dosage of testosterone in cases of angina, the following method of administration appears to be most effective in the average type of anginal cases, viz, 25 mg. of testosterone propionate is administered as bi-weekly intramuscular injections for a period of six to ten weeks (i.e. 12 to 20 injections in all). In the average case, it is necessary to repeat this course of injections two or three times a year for several years, depending on the duration and degree of improvement noted after this therapy.

The relation of 'response' to certain associated features.—In Lesser's opinion (1946) neither the age of the patient nor the duration of the disease has any bearing on the results obtained. In the present series of cases of angina, the results of testosterone therapy were somewhat better in the younger age groups (who are often examples of 'secondary' or 'post-thrombotic' angina) and in anginal cases of shorter duration.

The 'modus operandi' of testosterone therapy in anginal cases.—This has been discussed in detail by Waldman (1945). The following main concepts of the mechanism of testosterone therapy have developed in the medical literature on the subject: (1) The theory of *vasodilatation* which holds vasodilatation as the chief mode of action. This theory has been supported by Bonnell, Pritchett and Rardin (1941), by Hamm (1942), by Walker (1942) and by Strong and Wallace (1944). (2) The theory of '*establishment of a collateral circulation*'. This theory has been supported mainly by Lesser (1942) and to some extent by Hamm (1942). (3) By the '*correction of an androgenic deficiency*' (Bonnell et al., 1941). (4) By an '*improvement in cardiac muscle metabolism*' (McGavack, 1943; Waldman,

1945). According to Waldman, testosterone 'may mediate its benefit in part, through the correction and regulation of cardiac metabolism, permitting more muscular exertion before sufficient metabolites accumulate to produce pain'. (5) According to another school of thought, the beneficial effects of testosterone therapy, as reported in the literature, are explainable on the grounds of the cases selected for study being examples not of genuine angina pectoris but of an allied 'angina-like' 'functional' state or 'climacteric syndrome'. Goldman and Markham (1942) reported good results with testosterone in 6 of 7 cases of an 'effort syndrome', which they considered a complication of the 'male climacterium'. McGavack (1943) reported excellent results with testosterone in cases of so-called 'functional "climacteric" angina' but found the results completely disappointing in 'true "organic" angina'. Levine and Sellers (1946), after a study of testosterone propionate therapy in 24 cases, came to the conclusion that testosterone preparations are 'of definite value in relieving the chest discomfort sometimes associated with the male climacterium or the similar precordial ache of neurocirculatory asthenia' but of no value in genuine cases of angina pectoris.

Summary and conclusion

On the basis of his results of testosterone propionate therapy in 125 cases of 'proved' angina pectoris, the author is able to summarize his results as follows: (1) Of the 125 cases of angina pectoris, so treated, 42 were markedly improved, 52 moderately improved and 31 not improved at all. (2) The response to treatment when reported was usually more dramatic in cases of 'post-thrombotic' or 'secondary' angina than in 'primary' angina. (3) A complete, although temporary, cessation of anginal attacks, after testosterone therapy was noted in 33.6 per cent of the cases, a reduction in the frequency of anginal attacks in 75.2 per cent, a diminution in the intensity of attacks in 77.4 per cent, an increased capacity for effort in 76 per cent, improved exercise tolerance in 60 per cent and electrocardiographic improvement in 10 per cent. (4) After a statistical analysis of 376 cases of angina pectoris treated with testosterone (and including his own), reported in the literature up to date, the writer finds that 'improvement' has been reported in as many as 80.3 per cent of the cases.

Although not enough cases have been reported as yet to permit full evaluation of the efficacy of testosterone propionate in the treatment of angina pectoris, the clinical results so far noted by others as well as by the writer indicate that testosterone preparations are well worth a more extensive trial in cases of this type.

It must be emphasized, however, that treatment of angina pectoris with testosterone propionate is, by no means, a substitute for a reasonable or restricted mode of life and light diet,

both of which remain fundamental to improvement. Nor can one expect it to supersede the nitrates and other remedies when these are indicated.

Obviously testosterone preparations have a definite place in the treatment of angina pectoris and other coronary disorders.

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TROPICAL ULCERS IN MADRAS CITY

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A 'FOOT-INFECTION CLINIC' was specially opened in the Stanley Hospital, Madras, for carrying on investigation on the infections of

the foot, sponsored by the Indian Research Fund Association. During the course of the investigation a good number of tropical ulcers were seen and so a systematic study of this condition was undertaken. The ulcers were diagnosed as 'Ulcus Tropicum' by their indolent nature, foul-smelling profuse discharge, associated pain and tenderness, and above all, the presence of the fusiform bacilli and the spirochaetes in the discharge.

Incidence.—Tropical ulcers have been reported to be occurring in Madras since 1943 (Seshadrinathan, 1945; Rao, 1946). In the Stanley Hospital itself the incidence was high during 1943 to 1945, more than 30 cases a month on the average being admitted and treated as out-patients. Since 1946 there has been a fall in the incidence of these ulcers, the total number of cases referred to the 'Foot-infection Clinic' since December 1946 to the end of February 1948 being only 38.

Ætiology

Age.—No age was exempt from this affection. It was common among the young adults engaged in active work.

TABLE I
Age group

15 years and below	14
16 years to 30 years	15
31 years to 45 years	5
Over 45 years	4
			—
			38
			—

Sex.—Men were more affected than women in the ratio of 6 : 1. The average daily ratio of the new surgical cases in the out-patient department of the Stanley Hospital for the year 1947 was M : F as 3 : 1.

TABLE II
Sex

Males	32
Females	6
			—
			38
			—

Occupation.—People engaged in hard labour and living in insanitary surroundings were more prone to this affection than others (19 out of 38 cases).

Five of the patients had no house to live in and were living on the pavements of the streets.

TABLE III

Occupation

Hard labour—			28
Coolies ..	14	Others—	
Handcart or rickshaw pullers ..	2	Students ..	3
Blacksmiths ..	3	Beggars ..	2
	—	Mechanic ..	1
	19	Salesman ..	1
No occupation—		Compositor ..	1
Above 60 years ..	2	Tea vendor ..	1
Below 12 years ..	7	Cook ..	1
	—		—
	9		10
	28		—
		TOTAL ..	38

Duration.—The majority of cases came with a duration of a fortnight to a month (19 out of 38 cases).

TABLE IV

Duration

1 week and less	2
1 to 2 weeks	3
2 weeks to 1 month	19
1 to 2 months	3
2 to 4 months	6
4 to 6 months	3
6 months and above	1
No definite information	1
			—
		TOTAL ..	38
			—

Seasonal influence.—The general experience was that the ulcers occurred maximum during and immediately after the monsoon months. The monsoon failed in Madras in 1947 and it is possible that the decreased incidence may have something to do with this.

History.—In 14 patients, the ulcer started after a minor injury or abrasion. An equal number developed a small eruption to start with. Due to itchiness it was scratched resulting in an ulcer after infection. It is possible that these eruptions might have developed subsequent to a mosquito or an insect bite but no definite history was forthcoming substantiating this view. Two cases started as paronychia of the toes and later developed infection of nailbed whereas five others developed infection of nailbed consequent to trauma. These cases presented the characteristic features of a tropical ulcer on admission. Two cases had ulceration of the whole of the terminal phalanx of toes after an injury. One case had fungus infection in the interdigital space and subsequent to trauma developed extensive ulceration in the spaces

TABLE VIII

Size of ulcer	SUCCESSFULLY TREATED WITH PENICILLIN		SUCCESSFULLY TREATED WITH MARFANIL POWDER	
	Number of ulcers	Time taken to heal on average, days	Number of ulcers	Time taken to heal on average, days
Less than one inch in diameter ...	17	10	3	13
One inch or more in diameter ..	13	28	2	40

TABLE IX

Drug used	Number cured (patients)	Number relieved (patients)	Number otherwise discharged	Total number of patients treated
Penicillin alone	16	6	5	27
Marfanil alone	3	1	1	5
Double ulcers with different dressings	1	2	3	6
Total number of patients ..	20	9	9	38

burning sensation at the area which lasted for over half an hour.

Whenever *B. pyocyaneus* or *B. proteus* was co-existent in the ulcers, response to penicillin was poor. When the case was switched on to marfanil powder after preliminary penicillin dressings, the ulcer began to heal rapidly. Marfanil was found to be effective against *B. proteus* and *B. pyocyaneus*.

Dressing with marfanil caused burning sensation whereas dressing with penicillin was absolutely free from pain. Moreover, the cost of penicillin is low whereas the cost of marfanil is high. We are finding that the penicillin is the drug of choice because of its low cost and its efficacy in the quick healing of the ulcers and the painless nature of the dressings.

Our thanks are due to the Principal, Stanley Medical College, Madras, for allowing us to carry on bacteriological investigations in the Department of Bacteriology.

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LEGENDS ACCOMPANYING FIGURES

- Figure 1.—Tropical ulcers—multiple, two days' duration:
(i) Anterior aspect of the middle third of the left leg—note the thin sero-sanguineous discharge.
(ii) Over the dorsum of the foot. Both non-traumatic in origin.
(iii) Terminal part of the second toe. This one is of 20 days' duration—traumatic in origin.
- Figure 2.—Tropical ulcer—one month's duration. Developed as a small eruption to start with on the outer and anterior aspect of the lower third of the right leg.
- Figure 3.—Ulcer shown in figure 2—healed in 26 days. Note the faint scar.
- Figure 4.—Early ulcer lower third of outer aspect of the leg. Note the characteristic slough.
- Figure 5.—Tropical ulcer on the dorsum of the left foot. Note the sloping margins towards the centre and the saucer-shaped appearance. Traumatic origin.
- Figure 6.—Tropical ulcer over the metatarsophalangeal region.
- Figure 7.—Early ulcer over outer malleolar region.
- Figures 8 and 9.—Double ulcers in the right foot—one over the medial malleolus and the other over the little toe.
- Figure 10.—Spreading tropical ulcer on the leg—note the extending upper margin and pale granulation tissue in the floor.
- Figure 11.—Tropical ulcer over the region of the patella and the lower part of the thigh—rather an uncommon situation.
- Figure 12.—Ulcer over the outer aspect of the lower third of the left leg—note the discharge mixed with blood streaks and the appearance of the ulcer and its margins.
- Figure 13.—An ulcer on the upper and outer aspect of the calf—note the excessive discharge.
- Figure 14.—Ulcer on the outer margin of the heel of more than two months' duration. Note raised margins and scanty discharge and healed scar of an old ulcer lower third of the same leg.
- Figure 15.—Big chronic ulcer on the posterior aspect of the heel over the region of the insertion of Tendo achillis.



Θ
Fig. 1.

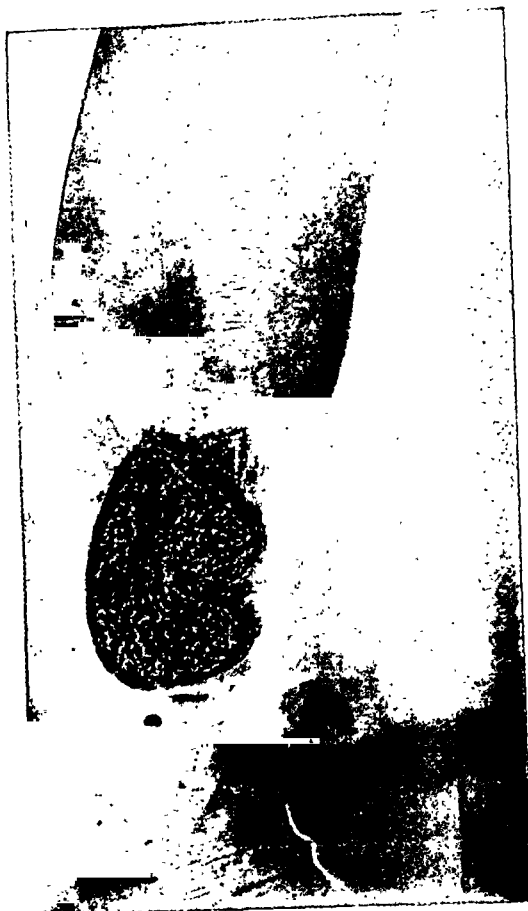


Fig. 2.

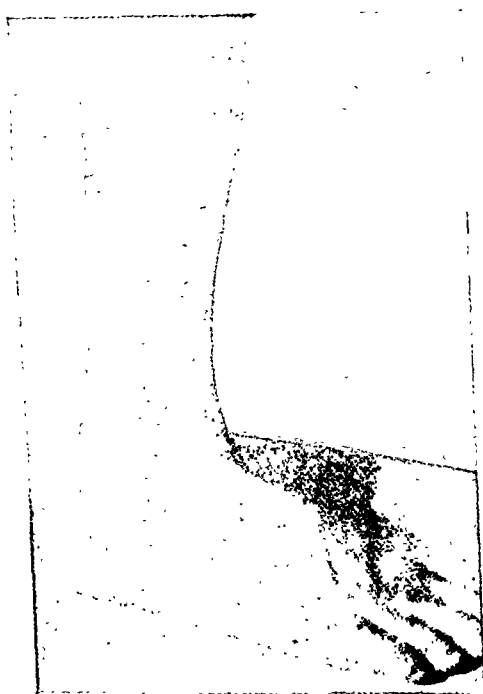


Fig. 3.



Fig. 4.



Fig. 5.



Fig. 6.



Fig. 7.

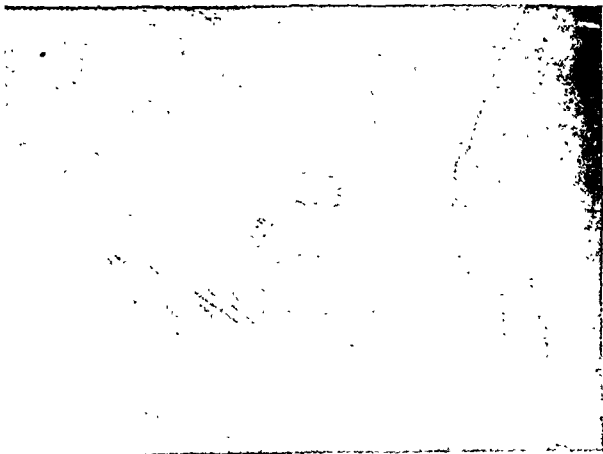


Fig. 8

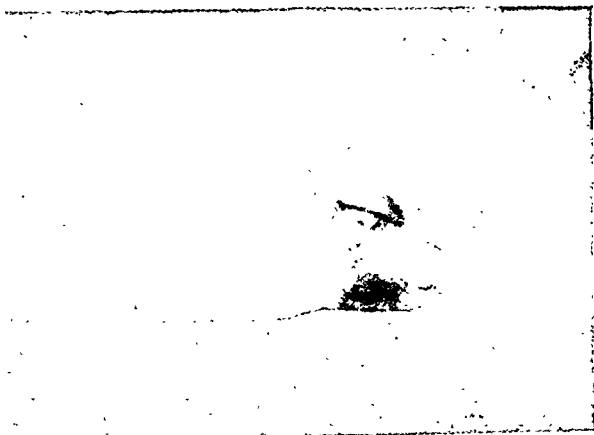




Fig 11.

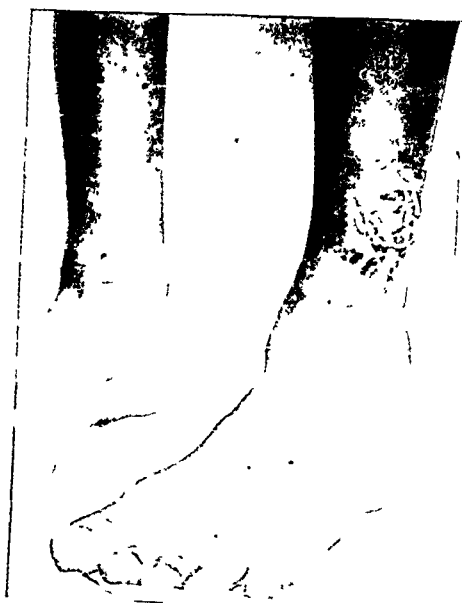


Fig 12

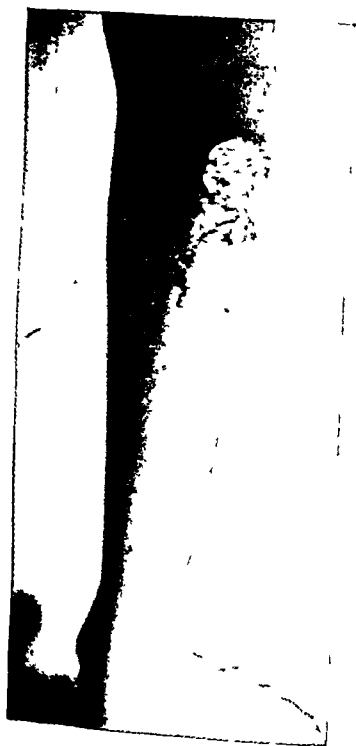


Fig 13.

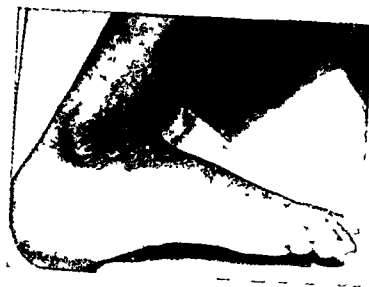


Fig. 14.



Fig 15.

SOME OBSERVATIONS ON ATLAS AND
AXIS VERTEBRÆ OF THE PUNJABEES

By INDAR JIT, M.S.

and

M. A. SHAH, M.S.

(Formerly of the King Edward Medical College,
Lahore)

No statistics are available as regards various measurements of atlas and axis vertebræ of Indians. The following work was done on the vertebræ of the known adult Punjabee skeletons obtained from the dissection-hall subjects of the Medical Colleges of Lahore and Amritsar during the years 1944-48. Twenty complete skeletons, 20 separate atlas and 20 separate axis vertebræ were measured. The measurements are given in tables I, II and III separately.

The following table shows a comparison with the findings of the previous workers in other countries as regards transverse and antero-posterior measurements of atlas vertebræ :—

The table shows that the average Punjabee atlas vertebra is 2.45 mm. shorter in transverse and 1.92 mm. in antero-posterior diameters than the European bone and slightly greater in size than that of Australian aboriginals. The posterior arch is fairly well developed as seen in the Europeans and is not a 'very narrow bar of bone'.

Axis vertebræ

The transverse processes can always be seen from above and are not hidden from view by the superior articular processes as in the case of the aboriginals of Australia. The average inter-transverse width in European vertebræ is 55 mm. (Cyriax, 1920), and according to Jones (1938), only 45 mm. in the Australian aboriginals, but in our series it was found to be 52.99 mm. We found the average antero-posterior diameter to be 48.02 mm. as compared to 50.59 mm. in Europeans and 41.7 mm. in the aboriginal vertebræ.

Name of worker	Race	TRANSVERSE DIAMETER		ANTÉRO-POSTERIOR DIAMETER	
		Average	Variation	Average	Variation
Cyriax (1920)	Europeans	78.7	63-90	45.41	30-53
Jones (1938)	Aboriginals (Australians)	72.5	68-80	42.2	38-47
Present workers	Punjabees (Indians)	76.25	66-87	43.49	38-50.5

(Measurements are given in mm.)

TABLE I
Complete skeletons

Serial number	ATLAS		AXIS							
	Diameter		Diameter		Neural canal		Distance of transverse process from body when seen from below		Direction of canal for vertebral artery	
	Transverse	Antero-posterior	Transverse	Antero-posterior	Transverse diameter	Antero-posterior diameter	Right	Left	Right	Left
1	73.5	41.5	56	47	21	18	6	6	Oblique	Oblique
2	75	43	50	49	22.5	18	0	0	Right-angled	Right-angled
3	72	40	50.5	41	20.5	19	0	0		
4	74	46.5	53	50	25	19	6.5	3	Oblique	Oblique
5	74	38	45	37	20	16	2	5	Right-angled	Right-angled
6	77	44	56	50	22.5	17.5	6	6	Oblique	Oblique
7	71	45	55	50	25	19	2	2	Right-angled	Right-angled
8	78	42	45	45	22	19	0	5	Oblique	Oblique
9	71	44	54	45	23	18	4	4	Right-angled	Right-angled
10	75	50.5	48	46	21	17.5	5	3	Oblique	Oblique
11	81	47	52	47	20	17	0	0	Right-angled	Right-angled
12	75	43	56	48	21.5	18	4	4	"	"
13	81.5	45	55	49	22	20	6	6	Oblique	Oblique
14	69	39	53	47	22	20.5	5	5		
15	80	44	49	53	22	19	4.2	4.2	Right-angled	"
16	84	44	55	50	24	20	2	2	Oblique	"
17	78	44	55	47	22	18	5	7	"	"
18	77	45	55	51	23	20	3	3	"	"
19	77	44	54	49	23	19	0	0	Right-angled	Right-angled
20	71	43	49	50	22	18	4	0	"	"

TABLE II
Separate bones

Serial number	ATLAS	
	Transverse diameter	Antero-posterior diameter
1	79	46
2	72	40
3	74	40
4	70	40
5	80	46.5
6	72	44
7	75	45
8	87	45
9	82	43
10	86	49
11	71.5	43
12	85.5	49
13	80	42.5
14	66	40
15	69	40
16	77	39
17	79	46
18	77	46
19	79	41
20	75	42

From the above measurements it can be calculated that the average Punjabee axis vertebra falls short of the European standard in the two diameters by 4.58 mm. only, hence no special or marked reduction in the size of

axis vertebræ is seen. In the Australian aborigines, according to Jones (1938), the axis was shorter by 18 to 19 mm. as compared with the European bone.

Neural canal

In European bones the average transverse diameter was 22.5 mm. with 55 mm. inter-transverse diameter as compared to 22.2 mm. in the aborigines with 45.2 mm. inter-transverse diameter. In our series, average width was 21.86 mm. with 52.99 mm. of inter-transverse diameter, showing thereby that the smallness of this diameter is quite proportionate to inter-transverse diameter. Macalister (1894) found that the shape of the vertebral canal in the aborigines was circular. In our series the shape was always found to be 'cordiform' as seen in the European bones. Our average antero-posterior diameter was 17.69 mm.

Site of the foramen transversarium

In Europeans the foramina are found to be situated at some distance from the body, no measurements having been given by the previous workers. According to Jones (1938) the foramina were situated immediately along the sides of the body and the canals for the vertebral arteries took right-angled course in aborigines but in the Europeans the canals were oblique. In our series the findings were not uniform. In 6 vertebræ the canals were

TABLE III
Separate bones

Serial number	Axis							
	Diameter		Neural canal		Distance of transverse process from body as seen from below		Direction of canal for vertebral artery	
	Transverse	Antero-posterior	Transverse diameter	Antero-posterior diameter	Right	Left	Right	Left
1	54	48	21	16	3.5	3.5	Oblique	Oblique
2	55	49.5	22.5	18	3	3	"	"
3	51	50	22	15	5	7	"	"
4	57	55	25	18.5	7	7	"	"
5	60	52	23	16	7	7	"	Right-angled
6	50.5	46	21	17	6	6	"	Oblique
7	48	46	22	16	2	2	"	"
8	53	50	22	18	6	6	"	Right-angled
9	51	42	22	17	5	4	"	Oblique
10	49	44	21	16.5	5	5	"	"
11	58	51	22	16	0	0	Right-angled	Right-angled
12	57	50	21	18	4.5	4.5	Oblique	Oblique
13	53	53	19	18.5	0	0	Right-angled	Right-angled
14	52	45	21	17	4	4	Oblique	Oblique
15	50	44	21	16	4	2	"	"
16	50	45	21.5	14	5	5	"	"
17	57	51	21	15	5	2	"	Right-angled
18	55	47.5	20	18.5	0	3	Right-angled	Oblique
19	57	50	20	18	5	4	Oblique	"
20	56.5	51	22.5	18	2	2	Right-angled	Right-angled

found to be grazing both the sides of the body, but in other cases they were found to be at some distance when viewed from below, the distance measuring up to 7 mm. The distance in about 35 per cent of the cases differed on two sides while in the rest it was equal. In 3 cases, the canal was in touch with the body only on one side and was at a distance of 3 to 5 mm. on the other. The above finding shows that this observation is not uniform in the Punjabees and cannot be considered a criterion, positive or negative of this race. As regards the obliquity or otherwise of the canal, findings again are not uniform. It was right-angled on both sides in 12 cases, on right side alone in 3 cases and on the left side in 4 cases. In the rest the canal was oblique in direction. In all those cases where the canal was grazing the side of the body, or was very near it, the direction was right-angled, while in the other cases no definite rule can be stated. In some cases where the distance of the canal from the body was fairly large, the direction was right-angled.

Summary

1. Eighty atlas and axis vertebræ of the Punjabees were measured and it was found that on the average they were slightly but proportionately smaller than the European bones.

2. Axis was not found to be specially short as in the case of aboriginals of Australia.

3. As regards the distance of the foramen transversarium from the body, and the direction of the canal for the vertebral artery, the findings were not uniform. Most of the vertebræ (85 per cent) had the canals at some distance from the body and in 70 per cent of the cases the direction of the canal was oblique on one or both sides.

4. Seven vertebræ were seen where the canal was oblique on one side but right-angled on the other.

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TUBERCULOUS PERICARDITIS

By BALBIR SINGH

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PYRAH and Pain (1933) analysed 7,945 autopsies; there were only two cases of tuberculosis of the pericardium amongst 215 cases who showed pericarditis. Smith and Willius (1932) surveyed 8,912 necropsies at the Mayo Clinic; they found only 3 cases of tuberculous origin in 373 cases of pericarditis amongst these necropsies. Dible and Davie (1947) also

considered tuberculous inflammation of the pericardium as rather rare. Price (1941) and White (1937) however state that it is not so rare as is generally supposed. MacCallum (1928) states that tubercle bacillus is one of the common causative organisms in cases of pericarditis and Wells (1901, 1902) to whose work Pyrah and Pain referred states that he found 10 cases of tuberculous pericarditis in 1,048 autopsies. Incidence in India is not known to the writer but presumably it is higher than that in England or America because of a higher tuberculosis mortality rate of the population as is obvious from the meagre statistical data available in some of the big cities in this country.* In a series of 151 autopsies done as a pathologist in the army, the writer observed 5 cases of pericarditis. Two out of these five were of tuberculous origin.

Case reports

Case 1.—A Gurkha soldier, 25 years of age, remained in different hospitals in Persia-Iraq force from September 1941 to April 1942. Complained of intermittent temperature ranging from 97°F. to 104°F. with occasional afebrile periods of short duration. He showed pleural effusion on 16th March, 1942, which was tapped and 24 oz. of fluid were removed from the pericardium on 29th March, 1942. He developed well-marked cedema, enlargement of liver, prominence of jugular veins and cyanosis before he died on 6th April, 1942.

Post-mortem examination.—The pericardium showed fibrous adhesions to the adjoining pleura on the left side and was also adherent to the diaphragm. The pericardial sac contained 25 oz. of fluid which was clear and yellowish in colour. Surface of the heart as well as the inner surface of the parietal pericardium were covered by a thick layer of fibrinous exudate. A few hilar glands were enlarged caseating and adherent to the pericardium. Both the pleural cavities showed 10 to 12 oz. of straw-coloured fluid and the abdomen also showed 10 oz. of similar fluid. The liver was enlarged in size and its cut surface showed a mottling with dark and light areas characteristic of a nutmeg liver.

Histopathology.—Tuberculous granulation tissue with typical giant cell systems and patches of caseation were lying over the heart

* This applies to foci of industry only. The greed brings the country born and bred lads to the slums of the foci of industry, where they sicken and die of sheer discomfort plus any disease going. Tuberculosis is only one of the diseases. The slums are effective in giving a massive infection which overwhelms the patient. To small doses of infection he should be immune as a member of an ancient race. Our cattle are certainly immune. Even guinea-pigs in India are difficult to infect. When the sufferer goes home to die he takes the infection with him and deals it out as often as not in massive doses again to the members of his family (see Editorial, *I.M.G.*, **83**, 41).—EDITOR, *I.M.G.*

muscle fibres. Superficial to these was a layer of fibrin. Lymph nodes of a hilar gland showed infiltration by epithelioid cells and patches of caseation. The liver showed pathology of chronic venous congestion.

Case 2.—A Punjabi Muslim, 25 years of age, admitted to hospital with a complaint of fever that came on with rigor. Diagnosed as a case of benign tertian malaria. Intermittent fever continued after antimalaria course of treatment and diagnosed as pericarditis because of radiological and clinical evidence 11 days after admission. Signs and symptoms of cardiac failure became well marked in 30 days and he died on the 53rd day after admission.

Post-mortem examination.—The pericardium showed fibrous adhesions to the adjoining pleura and was adherent to the diaphragm. The pericardial sac contained 10 oz. of straw-coloured fluid. Surface of the heart as well as the inner surface of the parietal pericardium were covered by a thick layer of fibrinous exudate. Three hilar glands were caseating and were adherent to the pericardium. The abdomen showed 6 oz. of clear fluid. The liver was enlarged in size and its cut surface showed engorged vessels which were dilated and dark blue in colour. Intervening parenchyma of the liver tissue was rather pale.

Histopathology.—Tuberculous granulation tissue with typical giant cell systems and patches of caseation were lying over the heart muscle fibres. Sections stained with Ziehl-Neelsen stain showed acid-fast bacilli morphologically resembling tubercle bacilli. Superficial to the granulation tissue was a deposit of fibrin. The liver showed the picture of chronic venous congestion and in addition a few of the portal tracts were infiltrated with lymphocytes and a few others were completely obliterated by tubercles.

Comment

Clinical condition of these cases towards the end of their life as well as the basic histological change (tuberculous affection) found in them after autopsy were the same as were observed by Viswanathan (1945) in cases described by him as subacute constrictive pericarditis. He chose to call them subacute constrictive pericarditis, obviously because their history of illness was of a couple of months only and the two layers of the pericardium were completely adherent and constricting the venæ cavæ. The pericarditic pseudocirrhosis of the liver has been described and objected to. Adhesive pericarditis has been reported without perihepatitis or polyserositis and *vice versa*. Oertal (1938) reported that he observed cases on autopsy table whose heart was incased in a thick hyalin scar tissue incrustated by calcium salts but showed no symptoms during life. Development of granulation tissue and its ultimate replacement by scar tissue leading to

obliteration of the pericardial sac are a common sequence of events in pericarditis if resorption does not take place. Partial synechia had already developed in case 2 reported above and if the patient had lived longer he would have developed complete adhesion of the pericardial leaves. Viswanathan's cases showed the last stage in the resolution of the tuberculous exudate in the pericardium. It would be more rational to call all cases of pericarditis in which tuberculous ætiology can be demonstrated under the microscope as tuberculous pericarditis rather than using a nomenclature based on the duration of illness, anatomical condition observed on post-mortem examination and traditional considerations.

Summary

Two cases of tuberculous pericarditis in a series of 151 autopsies are described.

I take this opportunity to thank the Director of Medical Services (India) for permitting me to report these cases.

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CAUSES OF FAILURE IN TREATMENT OF AMÆBIC DYSENTERY

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HARGREAVES (1945) and later on Wright and Coombes (1948) produced evidence to show that secondary infection was an important cause of lack of proper response to anti-amæbic treatment. The prospect of curing amæbiasis seemed brighter in view of this knowledge. Many attempts have been made as a result of experience gained in World War II to standardize the treatment. Such lessons are embodied in the courses recommended jointly by the War Office (1946) and the U. S. Army Medical Department. In spite of the courses of treatments suggested and also the use of diiodoquin latterly, the response to treatment has been poor. An investigation was

therefore initiated to evaluate the causes of this poor response.

Most of the patients in this series are of the well-to-do class. But the incidence of the disease is very high in the general population as well. Relapse rates are very high in the cases followed up. Other workers notably Wright reported a relapse rate of 45 per cent which figure tallies with that of Liesham. Raspton's figures are higher still, for out of his 26 cases, 24 relapsed within 9 months.

Various views have been put forward from time to time to account for the intractability of the infection. Adams (1945) made the suggestion that the amœbæ became resistant to emetine as a result of inadequate treatment and so did not respond to further emetine therapy. Another suggestion put forward by the same worker ascribed unusual virulence to the amœbæ. Hargreaves (1945) investigated the possibility of a secondary bacterial infection being an important factor in the poor response to treatment. His observations have been found correct by many workers both in India and elsewhere. Wright and Coombes (1948) reported the presence of secondary bacterial infection in 41 per cent of their cases.

Hargreaves (1945, 1946) gave encouraging reports of results with penicillin in resistant cases. Wright and Coombes (1948) have also reported striking improvement sigmoidoscopically after penicillin administration. In these resistant cases the secondary pyogenic organisms became established in the diseased bowel wall and therefore before specific anti-amœbic treatment could be expected to succeed the secondary infection needed elimination. War Office (1946) recommends large doses of penicillin and sulphasuxidine for the purpose. Best results have been reported by giving 100,000 units of penicillin to start with and 33,000 every 3 hours until a total of two million units has been given, concurrently with the 5 gm. doses of sulphasuxidine every 4 hours until 80 gm. have been given. Such high dosages however are not necessary in the writer's experience in the control of individual attacks.

Other causes of failure in the Burma campaign have been suggested by various workers—notably Priest (1945) and Manson-Bahr (1945): (1) It is possible that an infection made emetine-fast as suggested by Adams yields less readily to other anti-amœbic drugs. (2) Conditions obtaining in the War Zone often did not permit the minutæ of treatment which is so essential for the management of amœbiasis. (3) Debilitated condition of the patients.

The experience of the present worker has not been happy as regards the relapse rate. The cases that could be followed up showed a high 'relapse' rate. Twenty cases were treated on the regime recommended by Wright and Coombes (1948) with slight modification but only 15 could be followed up. Out of this 15, 10 showed signs

of 'relapse' within 12 weeks of apparent cure. It was, therefore, decided to look more carefully in the discrepancies in the results of treatment of the present series. The treatment given was:—

Emetine gr. 1	E.B.I. gr. 3	Carbarsone (Lilly)
Days 1-3	Days 4-10	One pulvule
Sulphaguanidine		Days 10-20
Tab. 36		E.B.I. gr. 3
Days 1-3		Days 20-25

The diagnosis was made microscopically. At the time of first examination of the patients a careful history and physical examination were recorded and a fresh specimen of the stools examined. If the stool was found positive for cysts or vegetative *Entamoeba histolytica* the patient was put on treatment. If first stool was found negative the patient was given an aperient and his stool examined on the second day. In cases showing negative stool a daily stool examination was made for a period of one week. Acute cases were put on treatment on suspicion also but this series includes only the positive cases.

In addition to the examination of the freshly passed stools of the patients giving a history of more than one attack the stools of the members of the patients' family and kitchen servants were undertaken. The results are very significant, in that in 14 cases a 'carrier' or a cyst passer was detected in the patient's house.

Routinely attempts were made to isolate amœbic cysts from the fingers of patients.* Only one patient showed the presence of cysts. A similar investigation could not be carried out on the kitchen servants. Only in 5 cases the inmates of the patient's house gave history of dysenteric attack.

A suggestion: Amœbiasis a family problem

The results of treatment are highly satisfactory so far as an individual attack is concerned, but are very poor so far as a long-term cure is taken into consideration. It is suggested that neither the drugs nor a particular treatment regimen nor the resistance or virulence of the *Entamoeba histolytica* can be blamed for the so-called relapses. These are, it is suggested, cases of re-infection from patient's own fingers or from the fingers of the cyst passers who handle his food. It is, therefore, concluded that the treatment of amœbic infection cannot be satisfactory if it does not take into consideration the other cyst passers in the house. It is significant that these 'carriers' seldom give a history of dysentery nor do they suffer from other suggestive symptoms of this disease. Persons in the families or household of five patients gave a history of dysentery many years ago, but only in 4 families did any number of inmates suffer from suggestive complaints such as flatulent dyspepsia and occasional abdominal pain at the time of examination.

* Fingers are important because of post-defecation washing with fingers.—Editor, I.M.G.

Physical examination revealed caecal thickening and tenderness in nearly all (60) the cyst passers except 4.

Summary

1. An endeavour has been made in this preliminary communication to show that amœbiasis is not an individual's problem but a problem of the family and for the sake of treatment must be reckoned as such.

2. The cases of so-called 'relapse' are really cases of re-infection.

My thanks are due to the patients for permitting me the facilities to investigate other members of their household and to Dr. S. N. Lahiri, Principal Medical and Health Officer, G. I. P. Railway, for permission to publish this paper.

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SOME CONSTITUENTS OF NORMAL BLOOD IN CENTRAL INDIA PEOPLE

SERUM CALCIUM AND SERUM PHOSPHORUS

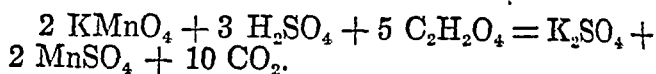
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THIS work is in continuation of our previous work already published in various journals (Gokhle and Lokre, 1947; Lokre, 1948).

The estimation of serum calcium and serum inorganic phosphorus is one of the estimations often asked for by physicians and surgeons. At present, normal values taken for the guidance in routine practice are those obtained by the workers on the Continent and the U.S.A. No such figures exist for India and hence this work.

There are several methods for the estimation of calcium. Most of these are based on the precipitation of calcium as calcium oxalate and then estimating the calcium as calcium carbonate and calcium oxide, or estimating oxalic acid by dissolving the precipitated oxalate in excess of hot, standard sulphuric acid and then estimating the oxalic acid so liberated by titrating against a standard solution of potassium permanganate. A recent and

more accurate method is to measure the volume of carbon dioxide evolved by gasometric method as per equation below and to calculate the calcium therefrom :



The method based on the estimation of oxalic acid was adopted (Clark and Collip, 1925).

In this estimation the precautions of washing the precipitate with 2 per cent ammonia water and then draining off the solution was very carefully observed. The last draining was done by keeping the centrifuge tube in an inverted position for a minute or so and then wiping out its mouth by a filter paper piece.

For the estimation of inorganic phosphorus contents of blood the methods used produce a blue colour by the addition of molybdic acid after reduction by a suitable reducing agent. The following are commonly used : (1) hydroquinone, (2) stannous chloride and (3) alpha-amino-naphthol-sulphonic acid. The last one was used by us (Fiske and Subbarow, 1925).

The blue colour produced in the estimation of phosphorus is rather light and hence special care was taken to compare the solutions 2 or 3 times and then recording the average which was used for the purpose of calculating the final result.

The donors were the students of the local medical school. These came mostly from the upper middle class. All of them were habituated to Central Indian vegetarian food and climate. Majority of them used to add now and then to their diet eggs or meat. They ranged between the ages of 20 and 25 years. The night previous to the taking of their blood, they were advised to have their usual diet but strictly warned *not* to take anything except tea in the morning they donated their blood. The centrifuge tubes and syringes used for this purpose were cleaned with dilute hydrochloric acid to remove the possible contamination with calcium carbonate present in the tap water used for washing. The acid was then removed with distilled water. The venous blood was drawn by using a dry syringe to avoid hæmolysis which interferes with the estimation of inorganic phosphorus.

The tables give the results recorded and the average values arrived at. Table I gives calcium and table II inorganic phosphorus.

Summary

The blood of 25 young, healthy normal persons of Central India were examined for their serum calcium and serum inorganic phosphorus. The average for calcium and inorganic phosphorus respectively are :—

Serum calcium 10.84 mg. per 100 cc. and serum inorganic phosphorus 5.01 mg. per 100 cc.

TABLE I
Calcium

Serial number	Age in years	Diet	Serum calcium mg. per 100 cc.	
1	21	V.	10.20	
2	22	V.	12.40	
3	21	M.	12.00	
4	24	V.	10.60	
5	22	N.	11.20	
6	22	V.	11.60	
7	23	M.	10.36	
8	24	N.	9.40	
9	22	V.	9.60	
10	22	M.	10.00	
11	25	M.	11.00	
12	22	M.	12.10	
13	22	M.	11.20	
14	25	M.	11.20	
15	20	V.	9.99	
16	22	M.	10.60	
17	22	V.	10.40	
18	23	V.	10.40	
19	23	V.	11.80	
20	21	M.	11.16	
21	20	M.	11.96	
22	24	N.	9.80	
23	24	N.	11.40	
24	24	M.	10.40	
25	21	V.	10.40	
Averages	22.40		10.84	Minimum 9.40 Maximum 12.40

TABLE II
Inorganic phosphorus

Serial number	Age in years	Diet	Serum inorganic phosphorus mg. per 100 cc.	
1	21	V.	5.08	
2	22	M.	5.28	
3	22	V.	5.16	
4	21	M.	5.28	
5	24	V.	3.88	
6	22	N.	5.32	
7	22	V.	5.64	
8	22	M.	5.04	
9	22	V.	5.20	
10	23	M.	2.84	
11	22	V.	6.72	
12	24	N.	3.92	
13	22	V.	6.12	
14	22	M.	6.00	
15	25	M.	5.32	
16	22	M.	5.12	
17	22	M.	5.12	
18	25	M.	4.84	
19	20	V.	6.00	
20	22	M.	6.08	
21	22	V.	4.48	
22	22	V.	4.40	
23	23	V.	4.60	
24	21	V.	3.92	
25	20	V.	3.90	
Averages	22.2		5.01	Minimum 2.84 Maximum 6.72

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SEROLOGICAL TECHNIQUE (contd.)

By S. D. S. GREVAL

LIEUTENANT-COLONEL, late I.M.S.

(From the Laboratory of the Serologist to the Government of India, School of Tropical Medicine, Calcutta)

STREPTOCOCCAL INFECTIONS :
SCARLET FEVER AND ALLIED
CONDITIONS

Dick test.—The test is analogous to the Schick test and performed in a similar manner. A 'skin test' dose of the toxin, available ready for use, is introduced intradermally in the left forearm, and a similar quantity of heated toxin is introduced similarly in the right forearm. The test dose in Great Britain is contained in 0.2 cc. and in the U.S.A. in 0.1 cc. of the liquid (as in the case of the Schick dose).

As the toxin itself is used in the test alcohol or any other disinfectant which will precipitate it is to be avoided. The syringe and needle should be boiled in distilled water and rinsed out with it. Further, the toxin is more stable than the Schick toxin and the heating for the control dose is done at 96°C. for 4 hours.

The reaction appears in 4 to 16 hours and begins to disappear in 20 to 24 hours. It may be :

Positive = susceptible. The slight flush measuring 10 mm. in diameter is taken as positive.

Negative = immune.

Negative-and-pseudo = immune. The pseudo reaction occurs in a very small percentage of children.

A positive-and-pseudo reaction does not appear to occur. Further, the pseudo reaction tends to appear later than the true positive (in about 24 hours), is less intense and fades more slowly.

The reading should be done in a bright light between 20 and 24 hours after injection. Only the flush and not induration is the criterion. The usual mistake lies in reading a positive reaction as negative.

The reaction is almost always negative at birth. About 20 per cent children at the age of 2 and over 70 per cent of adults are immune.

The test is also negative for days or weeks after the injection of scarlet fever anti-toxin.

Dick test toxin and the test fluid: (1) *The toxin.*—It is a sterile filtrate of a broth culture of a scarlatinal strain of *Streptococcus pyogenes*. The toxin contained is the *erythrogenic toxin* or *scarlatinal toxin*. It cannot be standardized so accurately as the diphtheria toxin. A skin test dose is 'amount which gives positive reaction in persons susceptible to scarlet fever and negative reaction in persons immune to the disease'.

Further, a satisfactory toxoid has not been made from the scarlatinal toxin. Addition of formol destroys both the toxin and antigenic properties. For immunization, therefore, the toxin itself must be used.

The toxin is very stable and addition to it of a buffer solution stabilizes it further.

2. *The control fluid.*—It is the heated toxin.

Prophylaxis against scarlet fever.—The toxin itself is used. Five hundred to one thousand skin test doses are injected subcutaneously at weekly intervals until a total of 80,000 to 100,000 has been given.

Reactions after injection of toxin may result in *scarlatinoid syndrome* which consists of generalized rash, malaise and vomiting. The symptoms disappear in 24 to 48 hours and need not cause alarm. Inclusion of 0.2 cc. of 1 in 1,000 adrenalin solution is said to decrease the incidence of the reaction.

Subjects with an allergic diathesis may not be given the toxin which is capable of producing rashes of erythema nodosum and polyarthritis.

The duration of immunity is of the order of months only.

Schultz-Charlton blanching test.—0.2 cc. of a 1 in 10 dilution of scarlet fever anti-toxin or 0.2 to 0.5 cc. of convalescent serum injected into the skin covered with rash, not more than 60 hours old, blanches the rash locally over a circle 20 to 60 mm. in diameter, within 8 to 24 hours. The blanching persists for 12 to 48 hours.

(When the rash is available the blanching of it should not be necessary for the establishment of the diagnosis.)

Specific serum treatment of scarlet fever.—At least 6,000 units are given in a single dose intramuscularly and repeated daily for 3 or more days if necessary. Spectacular results are reported.

It will be observed that the anti-toxin is believed to be useful in scarlet fever only, not in other affections produced by streptococci. This situation is comparable to the action of sulpha drugs in erysipelas: The drugs produce spectacular results in the latter affection only, not in scarlet fever or sore throat. There is evidence of competent observers to the effect, however, that in individual cases of streptococcal

septicæmia remarkable effects have been produced by the scarlet fever anti-toxin used in conjunction with other measures.

TREATMENT OF FILARIASIS BY LITHIUM ANTIMONY THIOMALATE

By S. RAJU AYYAR

Civil Assistant Surgeon, Tirukalikundram

IN the coastal areas of southern districts of Madras presidency filariasis is very frequently met with and is commonly seen in an endemic form akin to malaria. The disease though not responsible for mortality as much as malaria ranks equally with it in causing hideous and permanent disfiguration and suffering to the inhabitants of these areas. A general practitioner in these rural areas finds fairly high percentage of this disease in his daily out-patient work. Recently even the President of the Indian National Congress in his address at Jaipur session has made a reference to this disease amongst the diseases which the Health Department of the Union Government is to tackle immediately and earnestly. All members of the medical profession are fully aware of the extensive damage caused by this disease to the lymphatic system resulting in its varied manifestations such as lymphangitis, abscesses, lymph scrotum, chyluria, hydroceles, and elephantiasis. In spite of such common occurrence of this disease attempts to eradicate it both by preventive and curative measures are few and far between. Every medical man knows that this disease is an easily preventable one by mass education. It will be interesting to note that even the highly educated people in these areas have a very quixotic notion about the causation of this disease. One very often hears that this disease is due to bad drinking water, to eating vegetables grown in fields irrigated with sewage water, or to eating a variety of vegetables—green stews, etc. This is a sufficient proof of a want of interest in a disease which is not fatal though so prevalent. An average practitioner in the rural areas here is thus faced with a common disease which cannot be treated with certainty and thus jeopardizes his popularity.

In the course of my practice of over twenty-five years I have used almost all the remedies in the treatment of this disease that I came across both in advertisements and hearsay from other practitioners, with little or no benefit at all. Before using some of these remedies I have been trying to evaluate their efficacy by subjecting them to a crude method of investigation. The centrifugalized deposit of the fresh urine of a patient suffering from chyluria is put under the microscope and the solution to be tried is allowed gradually to come in contact with the actively moving *Microfilaria bancrofti*. With a low-power lens the effect of the drug on the move-

ments of the worm is observed; in some cases they become sluggish to start with and then become active again; in some cases no change in the movements occurs; but in the course of the use of the lithium antimony thiomalate (anthiomaline) the movements not only grow sluggish but stop altogether in certain instances. Even slight heating of the slide with a view to warming up and stimulating the worms has no effect. Thus concluding in my own way that the drug might serve the purpose more usefully than the other remedies that I had tried before I commenced to keep a record of observations on such cases. In this series of about 20 cases treated in the course of a year I have made the following observations and conjectures.

Lithium antimony thiomalate solution contains 6 per cent of an organic trivalent compound containing 16 per cent of antimony. The solution is administered by intramuscular route daily from half to two cc. according to age. The treatment is given for a period ranging from 4 to 6 months and even more. No untoward effect is generally complained of excepting for slight pain at the site of the injection which passes off in the course of the day. In few cases there may be slight fever, pain all over the body and particularly in the knee joints; nevertheless, the treatment should be continued unabated.

The selection of early cases of all types would help the practitioner to get courage and impetus to continue the treatment as the patients are sure to feel relieved. Advanced cases will be discouraging.

Case 1.—N. I., aged 52 years, a temporary resident of this place from Kancheepuram, consulted me for pain in the loins, fever attended with intermittent chilliness in the middle of August 1947. He was given ordinary diaphoretic mixture and within 24 hours he passed milky urine. On enquiry it was revealed that this was the second occasion and the previous one was about a few months ago. He was immediately put on sulphathiazole tablets 8 in the course of 12 hours and given 2 cc. of anthiomaline. In three days' time the urine cleared up, fever passed off and the pains in the loins had fully disappeared and in a week's time he was well again able to attend to his normal duties. He was given 50 cc. of anthiomaline in the course of two months. He is seen by me even to-day periodically having nothing to complain of and he says that he is getting a dose of it injected weekly for fear of any recurrence.

Case 2.—M. M., aged 45 years, an inhabitant of a village near the sea coast, was brought here in September 1947 with acute pain in the right inguinal region with very tender swelling, slight fever, restlessness, etc., resembling an obstructed bubonocoele. He was given an enema with no relief. Proper palpation was not permitted. The general condition was causing some anxiety and he was given chloroform and operated upon. To my utter disappointment only a lump of lymph exudate was found and the wound was

hence closed packed with sulphanilamide powder. He was put on sulphathiazole tablets as the previous case and anthiomaline was injected. The constitutional disturbances had cleared and the wound healed by first intention. The treatment was continued for 3 months and he is quite fit now.

Case 3 R. M., case 4 M. M., and case 5 G. M., all aged about 35 years.—These three cases had hydroceles definitely of filarial origin, verified on the operating table, and were operated upon during the year 1947. To prevent recurrence of constitutional symptoms and to facilitate quick healing of the wound and easy resolution of the serotal tumour injections of 2 cc. of anthiomaline were given daily for a week and then continued thrice a week for three months. All these cases are local ones and are being seen by me daily even to-day. They have nothing to complain of.

Case 6 N. M. aged 50 years, case 7 P. M. aged 49 years, and case 8 K. S. aged 18 years.—These three cases of filarial scrotum of varying sizes and of varying duration were all operated upon during the period of the trial of this drug. It has been my experience that in spite of careful selection of cases for operation of excision of scrotum in the apyrexial (quiescent) period, the constitutional symptoms flare up after the operation and mostly in a week's time, interfering with proper healing of the wound. As a sequence of this most of the patients are perforce bedridden for a pretty long time. In these three cases I commenced giving the injections from the third day onwards and in all of them I was able to remove the stitches from 10 to 12 days with slight or no raw area. The injections were supplemented with sulphathiazole tablets 4 a day. The injections were continued as usual for three months and in one case the patient is even now patiently coming for weekly injections.

Case 9 S. I. aged 38 years, case 10 S. A. 40 years, case 11 K. A. 30 years, case 12 M. A. 32 years, and case 13 K. A. 18 years.—These five cases are of early lymphangitis with slight painful lymphogranuloma either in the axilla, or in the epitrochlea, or in the groin. All these cases gave history of two or three previous attacks only. There was no apparent thickening of the skin present. In all cases there were constitutional disturbances of varying degrees. As in all cases obstinate constipation was the rule, an opening dose was administered for complete evacuation of bowels and tablets were started from the next day at the rate of 8 per day. The injections were given concurrently. All these cases got on well and they had in all 50 injections. Three cases are still continuing the injections bi-weekly.

It can be seen from these cases that the result of the treatment will give some encouragement and impetus only when early cases are selected. Therefore, selecting early cases for treatment

and at the same time advising the patients and relations to prevent infection by sleeping under the mosquito nets and to adopt sanitary methods for preventing mosquito breeding, the rural medical man may help the suffering public and the State in his own little way.

ERRATA

SEROLOGICAL TECHNIQUE (contd.)

By S. D. S. GREVAL

LIEUTENANT-COLONEL, late I.M.S.

(From the Laboratory of the Serologist to the Government of India, School of Tropical Medicine, Calcutta)

IN the above article published in the *I.M.G.*, 84, page 53, column 1, para 4, line 4

for '(2,000 to 5,000 units, again depending on weight', read '(2,000 to 5,000 units, depending on weight',

A REPORT OF 46 CASES OF ANÆMIA IN THE PUNJAB WITH SPECIAL REFERENCE TO NUTRITIONAL MACROCYTIC AND ADDISONIAN ANÆMIA

By P. N. CHHUTTANI, M.D. (Punjab), D.T.M. (Cal.)
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Lahore

IN the above article published in the *I.M.G.*, 83, p. 512, column 2, para 3, line 17, for 'new' read 'now', and last para, line 1, for 'They' read 'Two cases'.

A Mirror of Hospital Practice

A CASE OF HEPATIC APPENDICITIS

By B. N. SHARMA, M.B., B.S., Z.E.O., Z.S.

Inspector-General of Hospitals, United States of Rajasthan, Udaipur

DURING the course of my 15 years' surgical practice, I have removed numerous appendices with practically every type of anatomical anomaly and in all possible pathological states. But the case under reference was the first of its kind and, to my knowledge, one not so far cited in surgical literature. This shows that appendix is always a subject of un-ending interest. Even in a simple and carefully diagnosed case of appendicitis one must be prepared to meet all surprises—anatomical as well as pathological.

Case report

A Hindu male, aged 30 years, was admitted to the hospital on 13th September, 1948, with the following complaints:—

1. Pain in the right side of the abdomen.
2. Dyspepsia (eructations and acidity in the mouth), duration 3 years.

The pain was dull and more or less constant. It used to become aggravated after taking heavy meals. The patient could not remember having had an acute attack of this pain. Dyspeptic symptoms were also more or less constant and continuous for 3 years. He had vomits occasionally. He used to take some mixtures and light purgatives off and on.

The patient was a motor driver by profession. He was used to smoking and alcohol.

History.—G. C., infections about 7 years back. Malarial attacks now and then. No history of dysentery.

He was admitted into the hospital about 2 months back with the same complaint. He was suspected to be a case of peptic ulcer, so x-ray examination was done. Barium meal screening showed stomach contour, outlines and position normal, but hypertonic. Duodenal cap normal. Tenderness over appendicular area. Appendix not visualized.

On examination.—Temperature—normal, pulse—80, respiration—18. Bowels slightly constipated. General health of the patient satisfactory. Tongue clean, moist but slightly reddish in the central part.

Abdomen.—Slight tenderness on the right side of the abdomen, particularly in the right iliac fossa. No muscular guarding. No lump or any glands felt. Liver and spleen not palpable.

Urine: No abnormal ingredients.

Stools: A trace of mucus, a few leucocytes and erythrocytes present.

Blood: T.L.C.—6,400; D.L.C.—poly 56 per cent, lympho 38 per cent, eosinophiles 2 per cent, large mono 4 per cent.

Blood pressure: 130/90.

In view of the clinical picture and the x-ray report, diagnosis of chronic appendicitis was made.

Operation

Under spinal (stovaine) anaesthesia usual McBurney's incision about 1½ inches long was made. After muscle-splitting, the peritoneal cavity was opened. The caecum was pulled out and the appendix was found to be lying behind it. It was ensheathed in a membrane. This sheath was opened near the ilco-caecal junction and the root of the appendix was exposed. Even then the appendix could not be pulled out. Further examination revealed that the whole of the organ was lying behind and lateral to the caecum and adjoining part of the ascending colon. So removal was started by the retrograde method. The stump was invaginated and the main vessels in the mesentery were ligatured and cut. Even then the tip could not be reached. Hence the incision was enlarged upwards to follow the appendix. By careful clamp and ligature method, the whole of its length was

freed, and then the tip was found to be adherent to the peritoneal covering on the under-surface of the right lobe of the liver. Fortunately, this adhesion was not firm and thick. It was easily separated without any bleeding.

The raw surface created on the ascending colon and cæcum by removal of the appendix was then peritonized and the abdomen closed. The operation lasted for 35 minutes and was uneventful except for an initial fall in blood pressure which was restored after injection of coramine and pituitrin.

The appendix was about 8 inches in length and on slitting it open, chronic inflammatory changes could be seen in the lumen. There was no active ulceration or occlusion.

The further recovery of the patient was uneventful and he was discharged on 27th September, 1948.

The patient is healthy and has none of his previous abdominal complaints.

It was only after the operative findings that one could connect his peculiar symptoms, simulating gastric and duodenal disease. The condition of the appendix on dissection did not reveal any signs of marked pathological changes. In my opinion the patient's complaints were more due to the abnormal position of the appendix than to the inflammatory changes in it. I am adding the following in continuation of the above report.

The skin incision was enlarged to about 3 inches to 4 inches instead of the original 1½ inches incision. The incision in the external oblique aponeurosis and internal muscles was likewise enlarged. The internal oblique and transversalis muscles were cut across along the lateral border of the right rectus muscle in an upward direction towards the costal margin. I have found this method of enlarging McBurney's incision very helpful in cases where more space is required for exploration and further manipulations inside the abdomen. I have done ilio-colotomy in several cases through this incision and if still more space is required the medial leaf of the incised external oblique can be cut transversally. The cut will include the rectus sheath as well and sometimes, if necessary, it can be extended up to linea alba.

TWO ATYPICAL CASES OF GIARDIA INFECTION

By MAFIZ-UDDIN SIRKER, D.T.M. (Cal.)

P. O. Julrihat

THE short notes of the two cases described below are important and interesting as cases of similar nature are not as a rule encountered in private practice.

Case 1.—A Muslim male, aged about 30 years, complained of incessant and agonizing pain

round the umbilicus for past several years. He was treated outside for gastric, duodenal, intestinal and biliary colic but to no effect. For the past three years he had had continuous pain in his belly round the umbilicus. On examination, I found his general health deteriorated to a great extent. Blood: Hb 8 gm. Leucopenia, liver and spleen not enlarged. No malarial parasite in thin and thick film. Slight tenderness over the right iliac region.

I thought the condition might be due to chronic amœbic infection. He could not be persuaded to produce his stool for examination. He was treated for chronic amœbic dysentery but to no effect. At length he brought his stool for examination. It was examined consecutively for three days with practically the same result. It was full of giardia cysts. No ova of helminth. No amœbic cyst. He was at once placed on mepacrine treatment and the effect was most promising. Three such courses at an interval of two weeks were prescribed. Since then he has made an uninterrupted improvement in his general health too.

Case 2.—This case was interesting in that although it was a case of giardia infection yet, at the outset, it was very difficult to suspect the true nature of the case. A child, aged seven years, was brought to me for the treatment of bronchial asthma. He was treated outside for this complaint for some time past.

When first seen, he was in the grip of what looked like an attack of severe bronchial asthma with incessant unproductive cough. On auscultation, usual signs of bronchial asthma were heard. After palliative treatment his blood was examined twice to note whether it was a case of tropical eosinophilia. Eosinophils were not found to be increased. His liver was enlarged an inch below the costal margin. Spleen was not enlarged. No malarial parasite in thick or thin film. General health not deteriorated. Usual treatment was given for the above complaint but to no effect. His stool was subsequently examined. The only clue that led me to examine his stool was that he used to get one or two loose motions before paroxysm of asthma. The stool was full of giardia cysts—no ova of helminth—no amœbic cyst. He underwent three consecutive courses of mepacrine treatment at an interval of 2 weeks in between the courses. He has not had any paroxysm of asthma for the last several months and the enlargement of liver has diminished to an appreciable extent.

A RARE CASE OF MALFORMATION OF FŒTUS

By S. RAJU AYYAR

Tirukalikundram

In textbooks of obstetrics only a casual mention is made of a malformation of the type described in this note. It is called *Extroversion*

of *Viscera*. In the short description given in the books only a small portion of the wall of the abdomen is said to be absent and hence treatment is also suggested.

A Hindu woman, aged 35 years, from a village, belonging to weavers caste, multipara at full term of pregnancy, was admitted with a history of few hours' labour pains at home. Her general health was good and the previous children were healthy and alive. After the preliminaries had been gone through she was put on the board and a P.V. was made which revealed the absence of membranes. In their place some tense irregular surface was felt and with a speculum it was found to be purple in colour. The foetal heart was not at all audible in any of the areas. As the labour pains which had been weak became intense, good progress of the presenting part was made. In less than half an hour coils of intestine were delivered which presented purplish appearance of the strangulated hernia. Quickly followed the birth of the whole monster which was doubled up: that is, both the lower extremities were bent backwards. The monster presented the following appearance: The head was flattened but had the eyes, nose and mouth; both the upper extremities were well developed; the chest was present; no abdominal wall was present practically to anterior axillary line on either side; and lower extremities were well developed with toes but were folded backwards. The male sex organ was also well developed. All the internal organs of the abdomen were present. The placenta which was also delivered immediately after the birth of the monster had a small cord attached to the right side of the abdominal wall. The woman had an uneventful puerperium. No attempt was made by me to help the delivery excepting to keep a close watch on the process of delivery. My request for the monster was refused in spite of coaxing and persuasions on grounds of superstition for preservation.

A CASE OF ACUTE INTESTINAL OBSTRUCTION DUE TO VOLVULUS OF CÆCUM AND ASCENDING COLON

By P. R. SURI, P.M.S.

Civil Surgeon, Jalau

PATIENT H. M., aged 45 years, admitted with history of stoppage of faeces and flatus and repeated vomiting for 4 days previous to admission.

Examination showed enormous distension of the abdomen in all segments. Patient was obviously very ill. He had profuse regurgitant vomiting which had dehydrated him. Pulse rate 132 per minute, of low volume and tension.

Preparation

1. A soap and water enema was given to relieve the loaded rectum and thereafter flatus tube was passed.
2. Decompression and washing of stomach and upper intestines was done by means of Ryle's tube, as a preliminary before administering the anaesthesia.
3. Five per cent glucose and saline was given by drip method to combat dehydration and chloride depletion.

Operation

Abdomen was opened under general anaesthesia by a right paramedian incision in the lower abdomen and immediately there was a gush of turbid fluid and gas from the peritoneal cavity. An enormously distended segment of large bowel presented itself, which on further examination was identified as caecum and ascending colon. Both these were abnormally mobile and possessed a mesentery in continuation of the mesentery of terminal ileum. This mobile segment of caecum and ascending colon had undergone a torsion in a clockwise direction about 180. Twist due to long duration had undergone vascular occlusion with subsequent gangrene and perforation due to sloughing of caecal wall at its most distended portion. The volvulus was undone, but vascular occlusion had already rendered bowel non-viable which was not fit for replacement inside the abdomen. The gangrenous loop of the gut was exteriorized and brought to surface, a spigot was placed through the mesentery and Paul's tube was tied at the convex border.

Small intestine was divided 6 inches proximal to ileo-caecal junction and both ends were invaginated and closed. Side to side anastomosis was performed between ileum and the farthest segment of transverse colon and abdomen was closed after a careful mopping of the fluid and dusting with sterilized sulphanilamide powder around the exteriorized loop of large bowel. Patient was returned to ward with intravenous drip running, and was put on penicillin sodium 40,000 units every 3 hours, soluble sulphonamide 10 cc. twice daily and antigas serum.

In the subsequent course of the disease distension of the abdomen was a feature. Draining of fluid through the Paul's tube and soakage from the exteriorized gut continued. By the fourth post-operative day patient's general condition had improved sufficiently to stand resection of the exteriorized caecum and part of ascending colon which was done under general anaesthesia. The distal end of right colon was clamped, sutured and invaginated while the gangrenous portion was excised along with its mesentery. General peritoneal cavity was disturbed as little as possible during the above resection and cutting of its attached mesentery. Patient had an uneventful course subsequently.

except for suppuration of few stitches which healed by granulation.

The unusual and interesting points in the above case are as follows :—

1. Comparative rarity of volvulus of caecum and ascending colon and the existence of a mesentery of the ascending colon.

Ascending colon has to support and expel a column of liquid faeces against gravity. To do this it requires to be firmly fixed *in situ* to enable its muscles to contract with advantage. If unfixed this gut works at a great mechanical disadvantage resulting in stagnation of its contents and its falling down over the brim of pelvis.

2. The volvulus being so acute as to result in gangrene of the bowel, which was rather unusual.

3. Obstruction of 4 days' duration resulting in considerable fluid and chloride loss before admission to hospital.

4. Operation done at considerable risk and yet resulting in recovery of the patient.

Therapeutic Notes

NOTES ON SOME REMEDIES

XXVII.—DRUGS IN HELMINTHIC DISEASES, Part II

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Professor of Tropical Medicine, School of Tropical
Medicine, Calcutta

5. *Hexylresorcinol*.—It is a synthetic compound of pale yellow crystalline nature, probably the safest of the anthelmintics. It is very efficient in ascariasis and fairly satisfactory in oxyuriasis and ancylostomiasis. The drug can be given in freshly filled gelatine capsules or in the form of 'crystoids' anthelmintic pills with hard gelatine coating containing 0.1 and 0.2 gm. The dose is 1 gm. for adults and children over 12 years of age and smaller doses for younger children. The capsules must be swallowed without chewing as the drug has irritant properties and is liable to cause superficial erosion of the buccal mucosa. To be effective, it should be given on an empty stomach and food should be withheld for at least four hours after administration. A light evening meal consisting of soft foods only should be given the night before. Purgative immediately after treatment is not necessary, since this drug is not toxic. To clear away any dead worms which are not passed spontaneously, a saline purgative is given 24 hours after treatment. The drug is very

soluble in alcohol which should be forbidden during treatment.

Hexylresorcinol is also available as solution. An enema of a 1 in 1,000 solution (solution S.T. 37) is a useful adjunct to the oral crystoids in the treatment of threadworms.

It is a relatively non-toxic drug, but occasionally it causes gastro-intestinal irritation.

6. *Gentian violet (medicinal)*.—This is a reliable remedy for oxyuriasis and is the only drug known for strongyloidiasis. The best way to give it is in the form of 4-hour and 1½-hour enteric-coated tablets which are marketed in 3/20, 1/5 and ½ grain sizes. The dose for adults is 1 gr. thrice daily, one hour before meals with as little water as possible. For children, smaller doses are given. There is no serious reaction, but dizziness, headache, abdominal pain, nausea and vomiting occur in some patients; these are transient. If vomiting occurs more than twice after one administration of the tablets, the treatment should be temporarily discontinued. In pulmonary strongyloidiasis, a 0.5 per cent solution of gentian violet is injected intravenously; this causes a temporary bluish tint to the skin.

It is stated that gentian violet should be avoided in moderate or severe cardiac, hepatic, renal and gastro-intestinal disease and alcoholism.

7. *Phenothiazine*.—It is a close chemical relative of methyl blue and is more effective than gentian violet against oxyuriasis, but it has a very toxic action on the blood and effective anthelmintic doses may reach the toxic level in many patients. It is not recommended for general use.

Under close supervision it can be employed in refractory cases of threadworm infection or in patients who are intolerant of gentian violet. Only a refined product should be used and constipation must be avoided. It should not be used in infants less than two years of age.

Tablets of 0.5 gm. are available. The treatment lasts for 4 days. The dosage is given below :

Age, years	Per day, gm.	Total, gm.
2-3	.. 0.5	2
4-5	.. 0.75	3
6-7	.. 1.0	4
8-9	.. 1.25	5
10-11	.. 1.5	6
12 adult	.. 1.75	7

To small children, give it crushed in food or orange juice. Extra fluid should be given. Toxicity is manifested principally by nausea,

vomiting and hæmolytic producing severe anæmia.

8. *Diphenan*.—It is a white crystalline compound marketed in 0.5 gm. tablets used for removal of threadworms. The dose is 1.0 gm. thrice daily for one week for adults and proportionately smaller doses for children.

series (*I.M.G.*, 82, 408). Here we need mention only two compounds, fouadin (stibophen) and anthiomaline (lithium antimony thiomalate). These are used in the treatment of schistosomiasis and filariasis. Their dosage and method of administration are given in the table.

TABLE

List of anthelmintics with their dosage and uses

Drug	DOSE		How given	Mainly used for	REMARKS
	Adult	Children			
1. Santonin ..	3 gr.	1/6 gr. for each year of age.	As powder with calomel at bed time or along with chenopodium.*	Roundworms	
2. Oil of chenopodium	1 cc.	1 min. for each year of age.	In two divided doses (in gelatine capsules) at half-hourly interval.*	Do.	Maximum dose of 3 cc. not recommended.
3. Carbon tetrachloride	3 cc.	0.2 cc. or 3 min. for each year of age.	In capsules, with milk or with 1-2 oz. saturated solution of sodium sulphate.*	Hookworms, tapeworms, threadworms.	
4. Tetrachlorethylene	4 cc.	4 min. for each year of age.	Shaken up with 1-2 oz. of S.S. sodium sulphate.*	Do.	
5. Hexylresorcinol ..	1 gm.	0.1 gm. for each year of age.	In gelatine capsules.	Roundworms, tapeworms, hookworms.	Available as 'cystoids' anthelmintic or in freshly filled hard gelatine capsules.
6. Iodine violet ..	1 gr.	1/6 gr. for each year of age.	Thrice daily one hour before meals.	Threadworms, strongyloids.	Enteric-coated tablets. (Eli Lilly's Enscals) 3/20, 1/5 and 1 gr.
7. Diphenan ..	2 tablets, 0.5 gm. each.	1, 1/2 or 1/4 tablet according to age.	Do.	Threadworms	Avoid constipation. Use under close medical supervision.
8. Male fern, extract filicis liq.	45-90 min.	3 min. per each year of age.	In capsules or as emulsion in 3-6 divided doses at half-hourly intervals.	Tapeworms	Semi-liquids for two days before treatment and a dose of saline purgative in the previous evening.
9. Antimony salts : (a) Fouadin ..	1.5-5 cc. of 7 per cent solution.	Proportionately.	Intramuscularly	Schisto-somiasis, filariasis.	1.5, 3.5 and 5 cc. on 1st three days; then 5 cc. on alternate days. Total dose 45 cc.
(b) Anthiomaline	2-3 cc. of a 6 per cent solution.	Do.	Do.	Do.	On alternate days up to 20 doses.
(c) Myostibin ..	5 cc.	Do.	Do.	Do.	Daily for 20 doses.
(d) Pentavalent compounds.		Do.	Do.	Do.	See <i>I.M.G.</i> , 82, 408.
10. Hetrazan ..	0.5-2 mg. per kg. of body weight.	Do.	Orally	Filariasis	Three times daily before meals. An active filaricide.

* Given in the morning on an empty stomach.

9. *Male fern* (*aspidium, filix-mas*).—Male fern is a good drug for the common tapeworms. Extract filicis liquidum is used in a dose 45 to 90 minims.

10. *Compounds of antimony*.—These have been described in a previous article in this

11. '*Hetrazan*' diethylcarbamazine.—It is a piperazine derivative which was first found effective against the filarial parasite of the cotton rat. It has been tried in human filariasis due to *Wuchereria bancrofti* with very promising results. Further information is given later.

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Indian Medical Gazette

MARCH

ANTRYCIDE

THE Imperial Chemical Industries Laboratory, Manchester, has produced another wonder drug after paludrine. It is antrycide or 7555, a specific killer of trypanosomes of animals.

The team of workers had four leaders: Dr. F. H. S. Curd, ph.d., Dr. Garnet Davey, ph.d., Dr. W. A. Sexton, ph.d., and Dr. Charles Melville Scott, the only medical man in the team. Dr. Curd was killed in the recent Stockport train crash. He with Dr. Davey had discovered paludrine.

The success has been obtained by trial and error or 'enlightened empiricism'. Pharmacological studies were first carried on in small animals and later in calves. The work with calves was considered dangerous by the veterinary authorities who did not consider it safe to study trypanosomiasis in England (Editorial, 1949a). Arrangements were then made with the Colonial Office to carry out experiments in infected areas of Africa. The results of the experiments have been announced by the Colonial Office in conjunction with the Imperial Chemical Industries. The drug, a white crystalline powder soluble in water, cures all forms of trypanosomiasis in cattle, horses, camels and other animals (Editorial, 1949b). Further, it is able to prevent infection for 6 months. Furthermore, the injection is a simple matter and does not need a professional man. The production appears to be easy too: The makers hope to provide 2 to 3 tons of the drug this year. The composition and the mode of action of the drug have not yet been made known.

Apart from the strictly therapeutic triumphs, a prophecy of a new era of prosperity for Britain is made in the lay press (Robertson, 1949). Britain is going to open up Africa. The drug will make Africa a bigger cattle producer than Argentina. This means not only more security of food but also preservation of the soil which in Africa has been eroded by geographically restricted and haphazard farming due to the interference by the tsetse fly. As the fly will be defeated more soil will be available for extensive and scientific farming. It has been said that in the past the tsetse fly has done an invaluable service in saving great areas from becoming peopled, exhausted and ruined. It has preserved the virgin soil for the deserving posterity. The deserving posterity is now going to claim it.

Another possibility has been mentioned: As the tsetse fly is rather susceptible to the environment, the fact of settlement alone, rendered possible by the drug, may make the fly disappear and leave the land in the undisputed possession of the deserving posterity. When that happens a hitherto successful rival of *Homo sapiens* in the tropics will have been vanquished.

As to the synthetic drugs in general, it is only the beginning. It is no undue optimism to hope that before the century is out death from actual wear and tear of the mortal frame will be the normal termination of the human span of life.

After writing the account given above we had the pleasure of meeting Dr. L. B. Wevill, Chief of the Medical Division of the Imperial Chemical Industries, on a visit to India, through the courtesy of Dr. B. Mukherji, Director of the Central Drugs Laboratory, Calcutta. The impression we gathered is that the Imperial Chemical Industries are as optimistic and enthusiastic as the medical and the lay press but not as emphatic. The composition of the drug, we were told, is being published shortly in *Nature*. It is a coal-tar derivative. The action on the trypanosome appears to be specific and its mode must be one of interference with the metabolism of the protozoon. Further, to our great surprise, we learnt that the claim has limits: *Trypanosoma cruzi*, for instance, is not affected.

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Medical News

NEED FOR RESEARCH IN INDIAN MEDICAL SCIENCE: PROPOSED INTEGRATION OF INDIGENOUS AND WESTERN SYSTEMS

CHOPRA COMMITTEE'S RECOMMENDATIONS

(From a Press Note dated 20th February, 1949, issued by the Press Information Bureau, Government of India, New Delhi)

'THERE is urgent necessity for inaugurating research in Indian medicine so that it may, in an abundant measure, contribute to the corpus of medical science and art. By research, Indian medicine, which has been static for many centuries, will once again make its contribution to the welfare of the people of this country and of the world,' says the Report of the Committee on Indigenous Systems of Medicine which has just been published. The Committee was appointed by the Government of India in December 1946 under the chairmanship of Colonel R. N. Chopra.

The following is a brief summary of the Committee's more important conclusions:—

Medical relief afforded by Western medicine in India at present is extremely inadequate, says the Report. Indian medicine, in spite of its static condition, is still largely practised in India. There is

demand for it on the part of large and varied sections of the population. It helps to fill the big gaps in the present State-sponsored and State-maintained systems of Western medicine.

SYNTHESIS OF MEDICINE

The Committee are of the opinion that while Indian medicine can take much of practical value from the Western medicine, especially in the fields of surgery, obstetrics, structural physiology, pathology and diagnostic methods and appliances, the latter can also learn much from the philosophic background of Indian system, its comprehensiveness, the importance it attaches to the soil factor and dietary, its generalization of principles and the knowledge of truth gained by the use of supra-sensory perception.

The Committee do not believe that there can be separate systems of Western or Indian medicine. Science is universal and medical science is no exception. The so-called 'systems' merely represent different aspects and approaches to medical science as practised in different ages and in different parts of the world. The aim of all is the maintenance of health, and prevention and cure of disease. Anything of value emerging from these should be integrated and utilized for the benefit of humanity without reservation.

Such a unified system will give our people the benefits of all the advances that Western medicine has made and will provide them with a system more in keeping with their habits, tastes and requirements and which from its comparatively cheaper medicines will be more suitable to their economic circumstances.

INTEGRATION PRACTICABLE

The Committee are of opinion that the integration of Indian and Western systems of medicine leading to synthesis is not only possible but practicable and recommends that immediate steps should be taken in this direction.

The first step will be integration of the courses of study by arranging curricula in such a way that whatever is weak in one system is supplemented and strengthened by the strong points of the other system or systems. The second step will be teaching of each subject by the same teacher, instead of by separate teachers as now, giving the students a unified view of the Indian and Western medicine. The final step will be in the field of research where experts of Indian and Western medicine will work side by side, checking and verifying the various hypotheses and theories, either rejecting or harmonizing them. If the theories are such as could neither be rejected nor reconciled, they are to be used as parallel hypotheses.

Just as Western medicine is being taught in the colleges of Indian medicine, chairs of Indian medicine should be established in the colleges teaching Western medicine.

To facilitate the integration of teaching and studies the following steps should be taken simultaneously : (i) improvement in the basic education of the entrants; (ii) compilation of unified textbooks giving integrated versions of Indian and Western medicines; and (iii) training of special teachers for integrated studies.

SUPPLY OF TEACHERS

The first source of supply of teachers for integrated studies will be from the present schools and colleges of Indian medicine. Promising graduates of both systems with proper training will form the second source of supply to the future colleges provided good prospects are offered to them. The students should have working knowledge of Sanskrit or Arabic for Indian medicine and sound knowledge of English and basic modern sciences—chemistry, physics and biology—before starting professional studies.

ILLOGICAL OBJECTIONS

One objection raised against integration is that it will give rise to mental confusion in the student but

if the teachers and the taught are of the right type this should not occur. The other objection is that the integrated studies cannot be completed in the time specified for the course.

If the syllabus is properly worked out and a lot of unnecessary details eliminated, as is now being proposed in America and has also been recommended by the Health Survey and Development Committee, there should be no difficulty in completing the integrated course within the specified period.

WIDER EDUCATION

The conception of education to be given to a medical practitioner must be considerably altered and enlarged so that he not only has knowledge of technical subjects, but also a general background of sociological subjects. In other words, he should have the fullest opportunities for the development of scientific and humanistic talents to enable him to be a friend, philosopher and guide to his patients.

The curriculum of studies should be so arranged as to give the student adequate knowledge of Indian medicine with essentials of modern Western medicine, particularly in those branches where Indian medicine is deficient, to make him fitted for modern conditions of practice.

NEW CURRICULUM AND TEXTBOOKS

The course of training should extend to five years. A short-term course of three years should be conducted for an interim period, till an adequate medical personnel is trained to work in the rural areas. A curriculum of studies, which should be uniform all over the country, has been worked and syllabus given in the Report.

The Government should set up a Board of experts for editing and publishing classical texts and compiling the right kind of textbooks harmonizing ancient and modern knowledge, first in Hindi in the case of Ayurveda, and Urdu in the case of Unani, and later to translate them into provincial and regional languages.

TRAINING FACILITIES

Teaching institutions should be adequately subsidized by the State and maintained at a certain standard. There should be at least one well-equipped and adequately staffed institution in each Province and State in which the teachers should be adequately paid so that they do not have to resort to private practice. Those institutions which do not come up to the standard should not be allowed to carry on with the work of instruction. Such institutions should, if possible, be grouped together into one good institution or used for relief purposes. All teaching institutions should also be centres for carrying out research in which both students and teachers should participate.

The permanent increase in the number of trained medical personnel will take a long time and, even if they are available at a distant date, these persons will settle by preference in towns and cities only, in spite of monetary inducements to settle in villages. The pressing problem of immediate rural medical relief will thus remain unsolved. The Committee, therefore, suggest that use should be made of the existing practitioners of Indian medicine by giving them necessary training in public health and other essential subjects.

MEDICAL RELIEF

According to figures collected by the Committee there are more than 200,000 indigenous practitioners in India and out of these it should be possible to get 25,000 to come forward for this training course during the next five years. In addition to this, there are about 4,000 of institutionally qualified practitioners. This number should be sufficient to man the primary village dispensaries so urgently needed. The following suggestions have been made : (i) a six months' course in the elements of public health, minor surgery, obstetrics, etc., be given to them; (ii) registered practitioners, who wish to take the course, be given a subvention at Rs. 30 per month; (iii) graduates of schools

and colleges of Indian medicine, who wish to participate in the scheme, be allowed to sit for the examination without taking the course; and (iv) those who pass the examination should be taken in the scheme of rural medical relief.

There should be common all-India standards of professional and technical education for health personnel and a stable continuous long-range health policy. To implement the scheme of providing the rural medical personnel, suitable textbooks should be written by an expert committee and made available in all provincial and regional languages.

THE THREE UNITS

A medical practitioner, trained according to the Committee's scheme, is to be put in charge of a rural dispensary to serve a population of 3,000 to 3,500 which will be the primary unit of medical relief. The secondary unit will be in charge of an institutionally qualified person with headquarters in a big village giving relief to a population of 10,000. This unit shall also supervise the work of primary units. The Panchayat Unit is to be a mobile unit with emergency equipment and nursing staff and serve a population of 50,000.

There should be adequate provision for in-patients in the taluk, district and presidency towns. These hospitals should provide relief in all the branches of medicine, be well equipped and manned by both practitioners of Indian and Western medicine, the latter doing surgical and obstetrical work and the former treating mainly with Indian medicine. This bilateral arrangement will be only for a short time—until the synthesis has been effected.

STATE CONTROL

The Committee consider that the time has come for the Government to deal with the matter of control of medical education and practice in a comprehensive manner and that the Government should set up a Special Committee to go into the matter so that an all-India system of control is evolved and, if possible, one single register for all recognized systems by a comprehensive act of the Central Government.

If the problems of health and medical relief are to be tackled on a national footing, the State should take in its purview all the recognized systems in the country and legislate comprehensively for all, instead of by piecemeal provincial legislation.

In legislating for the control of recognized systems of medicine the following fundamentals should be kept in view: (i) adequate provision for the supervision of medical education of all the recognized systems, and of their teaching and treating institutions; (ii) registration of practitioners of the recognized systems; (iii) disciplinary control over practice; and (iv) setting up a consultative and advisory body on matters relating to public health and medical relief.

NATIONAL MEDICAL BOARD

To implement these proposals the Committee recommend the formation of a statutory body which may be called the National Medical Board. This Board should consist of two autonomous sections—the Indian Medical Council and the Council of Indian Medicine—one dealing with Western medicine and the other with Indian medicine. The provincial and regional branches should be affiliated to the Board which will also be an appellate authority over disciplinary actions on practitioners and institutions taken by provincial branches.

ELIMINATION OF QUACKS

Registration should be made compulsory for all practitioners in order to eliminate quacks and prevent the credulous public from being exploited. The register of practitioners of Indian medicine should be separate from that of the practitioners of Western medicine for the present. Later, when the standard of education in the colleges of Indian medicine improves

and the non-institutionally qualified fade out, the question may be reviewed and the desirability of having one register considered.

In the case of those who have no recognized academic qualifications, including well-known Vaidyas and Hakims, no distinction should be made in the register between the institutionally qualified and non-institutionally qualified. There should, however, be separate electorates for each of them for representation in the Councils.

NEED FOR RESEARCH

The Committee is convinced that there is a wealth of medical knowledge and experience in Indian medicine which needs proper investigation. It should be the purpose of painstaking research to salvage and collect this knowledge and experience and make it available to the country. The approach to research should be more in accord with the systems themselves, i.e. not only through observation and experimentation in the laboratory but also through meditational and intuitional means as practised by ancient servants.

Research, the Report says, should have a two-fold aim: (i) to clear Indian medicine of centuries of accretions of doubtful value and make its science and art intelligible to the modern mind, and (ii) to work for a synthesis of the Indian and Western medicines so as to evolve a unified system of medical relief and education, suitable for conditions of life in India.

Research should be conducted under the following categories: (i) Research in the fundamental doctrines of Ayurveda and Unani Tibbi; (ii) Research in the ancient literature on medicine; (iii) Clinical Research; (iv) Drug Research—Pharmacological, Pharmaceutical and Botanical; (v) Research on nutrition and dietetics; and (vi) Research on psychological aspects of medicine.

RESEARCH COUNCIL AND INSTITUTE

A Central Council of Research in Indian Medicine should be set up immediately whose functions will be analogous to those of the Central Medical Research Organization. The Council should consist of: (i) eminent practitioners of Indian medicine; (ii) representatives of scientific bodies, dealing with Indian medicine; and (iii) representatives of educational institutions where research in Indian medicine is being carried on.

The functions of this Council should be: (i) the formulation of policy of research in Indian medicine; (ii) the co-ordination of policy with that of other medical bodies and other research activities; (iii) the organization and general control and supervision over the Central Research Institute in Indian medicine which is to be established; (iv) stimulation of research in Indian medicine in the universities and educational institutions; (v) laying down of rules for the appointment of Directors and superior staff; (vi) appointment of the staff; (vii) appointment of Advisory Committees for research in special subjects; and (viii) allocation of funds and grants-in-aid for research work in the Central Research Institute and in other centres.

The progress of work in the various departments of this Institute should be published in a journal.

In the Central Research Institute provision should be made for post-graduate courses and training of research workers; research fellowship of the value of Rs. 150 per month should be established tenable for three years in the first instance to be extended to five years in special cases.

DRUGS AND MEDICINAL PREPARATIONS

There is great difficulty in correctly identifying many of the medicinal plants used in Indian medicine. This work should be taken up in all the provincial and regional centres and co-ordinated under the direction of the proposed Central Research Institute. The identification of medicinal plants will be helped to a great extent if a herbarium of properly identified and

preserved specimens of all known medicinal plants is established. Such collections already exist in the Forest Research Institute, School of Tropical Medicine, Calcutta, and Drug Research Laboratory, Kashmir.

For the extension of medical relief on rational lines, it is necessary not only to study medicinal plants but also to cultivate them for obtaining authentic and regular supplies. To do this successfully, a careful survey of these plants is necessary in order to determine suitable localities for their cultivation.

BOOK OF MATERIA MEDICA

As the existing literature on the subject is scattered and not easily comprehensible to students and practitioners, a proper textbook on materia medica should be compiled giving all the necessary particulars of different drugs by collecting and sifting all available information.

It is not possible to prepare an Ayurvedic Pharmacopoeia on the lines of Western Pharmacopoeias in the absence of the necessary data required for this purpose in connection with drugs.

The Central Research Institute should appoint an expert Committee to collect data, and consolidate it in the form of two lists—one of single important drugs and the other of important compound preparations. This will form the basis of a Pharmacopoeial List of Indian medicine. It should give all the information regarding the character, method of preparation, dosage and modes of administration with various vehicles.

As there is great difficulty in securing supply of genuine drugs for the manufacture of standard preparations, it is necessary that : (a) collection and distribution of crude drugs be carried out under a Government licence; and (b) those who sell crude drugs in the market be licensed and controlled.

A small Committee consisting of the representatives of the industry, vaidyas, hakims and a few modern pharmacists should be appointed to examine the requirements of the country in respect of indigenous drugs and finished preparations and suggest how best the control may be exercised.

Certain minimum standards should be laid down regarding the minimum staff, equipment and accommodation necessary for the efficient working of commercial manufacturing firms.

In respect of procuring excisable and poisonous drugs such as opium, ganja, alcohol, arsenic, etc., the facilities available to manufacturing firms of Western medicine should be made available to firms preparing Indian medicines.

COURSE FOR PHARMACISTS

Well-trained pharmacists in Indian medicine are essential for making available reliable preparations to the public and the Committee envisaged above should recommend ways and means to start a suitable course for training pharmacists.

The profession of pharmacy relating to Indian medicine should be controlled by proper registration on the lines of similar legislation enacted for the profession of pharmacy of Western medicine.

FINANCE

The many proposals made by the Committee would naturally involve additional expenditure to the Central and Provincial Governments and the States. The Committee are unable to make detailed recommendations in this regard, but urge that, in the existing health condition of rural India, medical relief should receive a high priority in provincial budgets.

A liberal Government grant should be given to selected existing educational institutions, for adequate accommodation, equipment and staff. A sum of Rs. 2 to 2½ lakhs as capital expenditure and Rs. 1 to 1½ lakhs as recurring expenditure should be given to each institution selected for the purpose by a Committee to be appointed for the purpose. The total cost

will be Rs. 20 to 25 lakhs and the recurring expenditure Rs. 10 to 15 lakhs annually divided among provinces and states.

The subvention of Rs. 30 per month for each trainee for the rural medical scheme will cost a sum of Rs. 1,20,000 to each Provincial Government for training 600 practitioners every year.

An officer should be appointed under the Health Ministry to hold charge of the section of Indian medicine and to be responsible for implementing the recommendations of the Committee in the work in the provinces and states.

WORK OF THE COMMITTEE

The Committee toured all the provinces and states, and met a large number of practitioners and institutional representatives of the various indigenous and modern systems of medicine in India, and also visited several Indian medical institutions and hospitals run by Government, states and private agencies in the country. The various questionnaires issued by the Committee elicited generous response from all parts of the country.

PRIMARY HEALTH CENTRE AT NAJAFGARH : FIRST OF ITS KIND IN INDIA

HEALTH MINISTER LAYS FOUNDATION-STONE

'Too long have the villages in India been neglected, too long have the Bhole Committee proposals remained mere paper recommendations', said Rajkumari Amrit Kaur, India's Health Minister, laying the foundation-stone of a primary health centre at Najafgarh, a village about twenty miles from New Delhi. 'This is an epoch-making event in the history of health services of India. May such centres multiply quickly all over the land', she added.

Amongst those present at the ceremony were Lady Mountbatten, Lady Pamela Mountbatten, H. H. the Princess de Ligne, wife of the Belgian Ambassador, representatives of the American Embassy and the United Kingdom High Commissioner's Office, members of the World Health Organization and officers of the Ministry of Health. A large number of villagers from Najafgarh and the surrounding areas thronged to witness the function. The Chief Commissioner and the Director of Health Services, Delhi Province, welcomed the Health Minister and the guests.

A miniature design of the proposed health centre and a health exhibition arranged for the occasion attracted much attention.

The first of its kind in India, this centre is being constructed in pursuance of the Bhole Committee's recommendations and will serve as a model for other similar centres elsewhere in the country.

It will have, to begin with, a six-bed hospital and a dispensary with a male and a female medical officer of health, nurses, midwives and other medical and public health personnel. The intention is to expand and equip this health centre with 40 beds during the next five years, to serve a population of over 20,000 living in 26 villages, within a radius of two miles. The medical officers in charge will carry out combined preventive and curative duties.

The medical officers and other staff of the health centre will, in addition to their duties at the centre, render medical and maternity services in the homes of the people, and will also educate the public in matters essential for the maintenance and promotion of health.

Housing accommodation for the health staff has been provided. A motor ambulance will be in use, and the question of providing an additional animal-drawn ambulance for villages which lack satisfactory communications is under consideration.

The centre is expected to start functioning in about a year.

Public Health Section

D.D.T.—AN IDEAL INSECTICIDE AND LARVICIDE

By B. L. CHOPRA, D.P.H., D.T.M. (L'pool)
Divisional Medical Officer, E. I. Railway, Kanchiapana.

RECENT award of the Nobel Prize for medicine to the Swiss scientist Dr. Paul Muller for his discovery of D.D.T. is an event of great importance. It was after many years of research devoted to synthetic insecticides, with the hope of replacing the vegetable insecticides by substances capable of being manufactured as required and capable also of modification to meet particular requirements, that Dr. Paul Muller of the firm J. R. Geigy A. G. of Switzerland discovered D.D.T. The early patents protecting its use as an insecticide date from March 1940.

Ideal insecticide

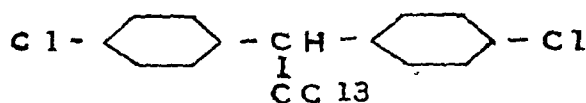
During the period of research the following qualities were aimed at for an ideal insecticide :—

1. Toxicity to insects of many types combined with safety when in contact with mammals and plants.
2. Stability in order that it may continue to kill for the longest possible period.
3. Power to persist in presence of sunlight, rain, growing plants and soil, etc.
4. Lack of stain.
5. No offensive smell.
6. Ease of manufacture.
7. No harmful effects on fabrics, metal and furniture.
8. Low cost.
9. Adaptability to many methods and purposes.
10. Pleasant aromatic smell and certain degree of repellent action.

Tested by these criteria, D.D.T. (dichlorodiphenyl-trichlorethane) is closer to the ideal than any other known insecticide. Only quality lacking is no. 10.

Chemical composition

As above stated D.D.T. stands for dichlorodiphenyl-trichlorethane. It may be expressed as



General properties of D.D.T.

D.D.T. can be used as a solution in some organic solvent or again after making solution in

that solvent it can be emulsified with water. Also as a dust it has been used. There are many possibilities of its dissolving in many solvents and then being emulsified by a number of different agents. Sometimes it can, after being dissolved in an almost non-volatile mineral oil, be emulsified and then sprayed on water. It will then float on water. As an alternative it may be dissolved in some much more volatile material and then used as a spray after being emulsified. In that case, after the solvent has evaporated, dry D.D.T. and traces of emulsifier are left behind. In this way it can be effectively used on the surface of the wall.

D.D.T. is known to be quite compatible with extracts of pyrethrum. The use of pyrethrum as an insecticide has been mentioned in an article published by me in March 1938 issue of the *Indian Medical Gazette* on antimalarial measures in railway area at Delhi. On account of its pleasant aromatic smell and certain degree of repellent action it exercises on certain insects, pine oil has been used as an adjuvant when using pyrethrum as an insecticide.

Approximate solubility of D.D.T. at 27° to 30°C. is given below :—

Solvent	Grammes of D.D.T. per 100 ml.
Cyclo hexanone	100 to 120
Ortho dichlorobenzene ..	63 to 71
Acetone ..	50 to 55
Carbon tetrachloride ..	46 to 48
Methyl salicylate ..	39 to 41
Ether ..	27 to 28
Pine oil (Hercules 'Yarmor 302')	15
Cotton seed oil ..	9
Kerosene, crude ..	8
Kerosene, refined ..	4

D.D.T. tends to be more soluble in the less highly refined oils.

Solubility in water is very low. D.D.T. is heavy and its addition to crude oil might produce a solution so heavy that it would sink in water. D.D.T. is so highly insecticidal that the solution in water cannot be considered to be harmless to such insects as mosquito larvæ.

In the year 1945 the Railway Board set up an 'ad hoc' committee of research under the chairmanship of the C.M.O., N. W. Railway. The committee tried to incorporate D.D.T. in paint with efficient action. A third class bogie was painted with such paint as an experiment, but the experiment was believed to be a failure, as particles of D.D.T. were no longer available for ingestion by mosquitoes. The committee, further, established that not all samples of

D.D.T. are satisfactory. Present-day commercial samples vary somewhat widely in their purity, depending on the process used in manufacture and on whether the material has been recrystallized. Much that is at present available has a purity of 60 to 70 per cent. The principal impurity (the ortho para compound) has been isolated and shown to be only slightly insecticidal. It has also been established that for accurate work one should either use chemically pure samples or state the amount of the pure para compound in the material which was used.

From the list given above of the solubility of D.D.T. it will be seen that D.D.T. dissolves better in crude kerosene than in refined kerosene.

Most effective D.D.T. is known to be obtained from the United States of America and other samples are known to be 60 per cent less effective. D.D.T. in oil is more effective than D.D.T. in dust. 100 per cent solution is obtained in cyclo hexanone but at present the price is hardly justified. According to Campbell and West (1944) American production had reached three lakh pounds per month when their paper was published in September 1944.

D.D.T. is stable in the presence of light, ultra violet, water vapour and boiling water. It is without effect on metals, fabrics, leather and dyestuffs. In view of its use, however, with organic solvents or emulsion, such a spray may do harm to paints and varnishes.

D.D.T. acts as a contact poison and its action on insects is generally slow probably due to its very low solubility in watery fluids.

Special applications

Uses of D.D.T. as an insecticide and larvicide against mosquitoes and those particular types of insects which are important to our society are given below :—

(A) Mosquitoes

(i) As a larvicide it will produce a less dramatic improvement and, unless care is taken to ensure that it is properly developed, it will meet the fate of paris green which has been recently discredited in many large areas. Application from the ground reduces the amount of oil needed from 20 gallons to half a gallon per acre. It might be said that the use of paris green similarly reduces the weight and cost of larvicide used. The labour of application remains much the same. Supervision is more difficult and consequently employment of more highly skilled labour is essential. There is physical difficulty in the application of such small quantities evenly over large water areas and the types of apparatus now in use are not quite suitable. Little reduction in cost or increase in efficiency will result if it is used as a mere substitute but this could be achieved if it was no

longer considered necessary to ensure application to every part of the breeding area or if somehow a prolonged larvicidal effect could be obtained. Prolonged effect in small water areas following the introduction of balls made of a plaster of paris sawdust mixture incorporating the larvicide has been needed.

The use of aeroplane for the distribution of D.D.T. in oil was originally regarded as a larvicidal measure. There is evidence that it is very effective specially on large bodies of water but it is found that some of the oily spray contaminates surfaces and kills many of the adult mosquitoes. Moreover, it does not only kill day-biting mosquitoes which might contact the spray particles while in flight but it also kills night-biters (*Anopheles*), which, presumably, pick up D.D.T. from surfaces on which they alight during the night after the spraying.

(ii) *Adult mosquitoes*.—Most sprays for use against mosquitoes or flies now rely on D.D.T. to kill the insects. Some pyrethrum extract may be added if a quick knock-down is desired. For spraying of passenger aeroplanes these sprays are now being used.

The effects of residual spraying against adult mosquitoes have been so good that it seems possible that this may prove to be the best method of using D.D.T. for routine malaria control in civil population. The main use of D.D.T. has been as a residual insecticide and of necessity practical work has been running alongside or even ahead of experimental work.

D.D.T. has been applied for this effect in the form of kerosene solutions, emulsions and as a dry dust. The results appear to be much the same but are less satisfactory with the dust. As a preliminary precaution, the oil used as a solvent should be tested to ensure that it is not repellent, a practical possibility which has been at one time a serious source of trouble.

It is considered that theoretically thorough spraying once every three months should suffice, but in practice under service conditions to derive maximum comfort and protection, monthly re-spraying is recommended.

Trials to ascertain the comparative efficacy of various preparations of D.D.T. as indoor residual sprays were carried out by the Malaria Institute of Delhi in seven villages in the Delhi rural areas. This work continued temporarily due to extensive flooding of the rural areas and on account of disturbances that took place in Delhi in 1947, and this work is being continued this year. Experience of work carried out by the Malaria Institute has shown that for indoor residual spraying, a stirrup pump fitted with a suitable nozzle is simpler and better than other type of spraying equipment.

(B) House flies

There is little published information on which one could precisely evaluate D.D.T. as a spray

against adult house flies. The following combinations have been known to be effective against adult flies :—

D.D.T. 0.10 per cent	+ Pyrethrine	0.03 per cent
D.D.T. 0.05 per cent	+ Pyrethrine	0.05 per cent
D.D.T. 0.10 per cent	+ Thanite	2.0 per cent
D.D.T. 0.10 per cent	+ Lethane	381.20 per cent

The above mixtures give a very high knock-down in 10 minutes or less, as well as a kill of 90 to 100 per cent. Used alone D.D.T. will give no knock-down but 80 per cent kill.

Residual films will probably prove even more valuable in fly control than sprays. The adult flies are susceptible to traces of dry D.D.T. in the surface on which it settles. There is also evidence available from different parts of the world that one application of the above mixture will keep a cowshed clear of flies for the duration of a European or North American summer. The method is applicable to restaurants, markets, latrines, screens and to almost any surface on which flies settle. A very minute dose is effective on glass, probably on account of the fact that D.D.T. crystals are readily detachable and all on the actual surface. It is, therefore, quite possible to put an invisible film on the inner surface of a window, and be free of the buzzing of flies for weeks.

D.D.T. in the form of a residual film is quite effective and this may, therefore, prove very valuable in tropical slaughter-houses, in the markets and so forth. It may also be sprayed on animals to kill the flies which contact them.

(C) Head and body lice

The essential point in dealing with an outbreak of lice on a large number of human beings is to use some insecticide which has a lasting effect. The Geigy Company in Switzerland were the first to discover D.D.T. for the control of head and body lice. They have been advertising from the later part of 1942.

D.D.T. dust experiments have been made. A cloth sleeve is slipped over the arm or leg of an experimental subject, lice and powder introduced into it and the ends fixed to the skin above and below with adhesive tape, results were examined after 24 or 48 hours : if all lice were dead, more were introduced and the experiment continued (sleeve and powder remaining in position) till insecticidal action of D.D.T. became very weak. D.D.T. showed itself very potent and much more lasting than other materials and further tests were carried out in which men's underclothes were dusted and then infested with several hundred lice. 10 per cent D.D.T. dust is now widely used. The effect lasts for 2 or 3 weeks and may kill lice after that, assuming that the person does not wash his garments. For men in winter clothes 1½ ounces per treatment suffice.

Very wide use of D.D.T. dust in the control of the epidemic of typhus in Naples early in 1944 was made. The method of application of the dust was by hand-blowers, dust being puffed up the sleeves and trousers' legs, down necks

and into the waists of shirts and trousers. This method is very quick and seems to have been proved effective.

An even more effective way of using D.D.T. in the control of lice is by impregnating garments which then become insecticidal and capable of killing lice even after wear for several weeks and several washes in hot soap and water. An addition of one or two per cent by weight of D.D.T. is all that appears necessary. This can be added to fabrics (cotton or wool) either from solutions in volatile solvents or from emulsions. The emulsions may be particularly valuable for they only require diluting to a particular figure after which a few garments can be 'louse-proofed' in a bucket.

Emulsions have been used to impregnate the hair of the head. A dose of 0.2 gramme of D.D.T. is quite enough for a week for this purpose.

(D) Bed bugs

Dry dust 5 to 10 per cent have been used successfully. In the circumstances which generally prevail in houses, dust is more likely to be removed than a spray deposit and therefore less likely to give a satisfactory lasting effect. The exact dose to be put down cannot be precisely defined. The more one puts down, the longer it will last. About 100 mg. per square foot is likely to be satisfactory and will kill any bugs which may be brought in for about three months. 5 per cent of D.D.T. in kerosene or 7 ounces per gallon may be used.

(E) Other domestic insects

Cockroaches appear to be somewhat resistant to D.D.T. Against fleas 5 per cent D.D.T. powder is effective.

Generally speaking, some ticks require high dose by the methods of application which have been used up to now. Further work on ticks may prove D.D.T. useful in prevention of tick-borne diseases, particularly tick-borne relapsing fever.

As to the clothes moths there is no detailed information available but it is generally believed that impregnated garments are moth-proof and remain so for a long time.

Most of the observations in the above article are based upon the use of D.D.T. in railway areas and hospitals at Ferozepore and Delhi. The writer was fortunate to get liberal supplies of D.D.T. through the courtesy of the military medical authorities in Ferozepore and Malaria Institute in Delhi. It was as early as the year 1944 that he started using D.D.T. in Ferozepore railway areas and this must be the first occasion when D.D.T. was ever used in any railway or civil area.

My thanks are due to Dr. S. S. Kent, Chief Medical Officer, E. I. Railway, Calcutta, for his permission to send this article for publication.

REFERENCE

CAMPBELL, G. A. and J. *Oil Col. Chem. Assoc.*, West, T. F. (1914). 27, 241.

THE INCIDENCE OF DELIVERIES AND CONCEPTION

By Miss JIWANLATA

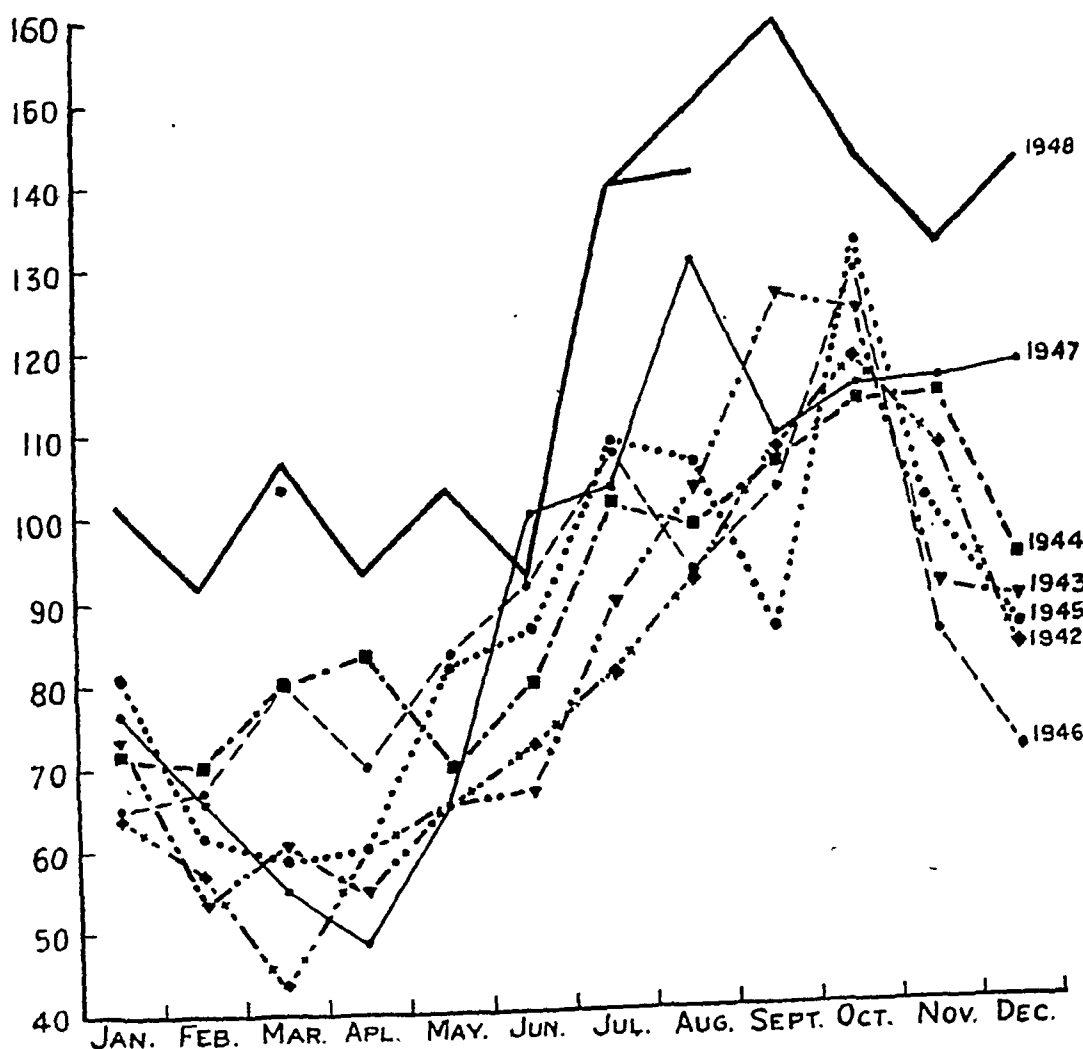
*Superintendent. Mrs. Girdhar Lal Maternity Hospital,
New Delhi*

BELOW are appended a table and a chart showing the incidence of deliveries according to months. It is, I think, every doctor's experience in female hospitals especially maternity hospitals that less deliveries take place in winter and more in autumn.

This study was undertaken with a view to finding out the correct variations. The record presented is of deliveries which took place between 1942 and 1948 in this hospital. These were mostly deliveries at full term. From this study it appears that the lowest incidence of deliveries is in the months of February, March and April and highest in August, September and October which means that conception takes place more often in the months of November, December and January and least often in the months of May, June and July.

Similar studies by others may perhaps throw some light on conception.

CHART



TABLE

Incidence of deliveries according to months

	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1942	67	57	42	60	67	73	80	95	109	119	108	81
1943	74	55	60	53	67	69	91	105	128	116	91	90
1944	72	71	79	84	68	82	104	98	107	116	115	87
1945	82	64	59	60	84	86	107	103	87	133	103	87
1946	66	69	80	68	85	93	108	94	104	130	87	72
1947	75	63	55	49	66	102	106	131	98	116	115	119
1948	106	92	108	93	101	94	140	152	162	145	133	145

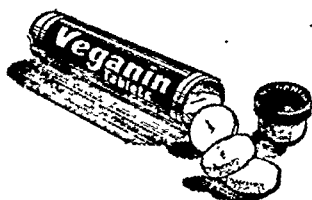
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The Indian Medical Gazette Fifty Years Ago

MEDICAL PRACTICE AMONGST THE MONGOLS

(Reproduced from the *Indian Medical Gazette*,
Vol. 34, March 1899, p. 100)

A FRENCH army surgeon, J. J. Martignon, resident at Peking, has given an account of Mongolian medicine based on information received from a native who was for a time physician to the living Buddha of Ourga, an important town some 800 miles north-west of the Chinese capital. Medicine among the Mongols is a monopoly of the Llamas. There is a school of medicine at Ourga, where, after a prolonged course of philosophy and Buddhist theology, three years are given to the study of the art of healing. Mongolian medicine is largely derived from Chinese, and through that, from European medicine as it was two centuries ago. The European strain comes from the old treatises translated into Chinese by the Jesuits in the reigns of the Emperors Kien-Long and Kan-si. Mongols do not dissect, and their knowledge even of the position of the internal organs is vague. The number of diseases is fixed at 440. Works on medicine are very numerous, the chief one being a kind of encyclopædia, entitled 'Khlantap', which is divided into eight sections and consists of 156 chapters. Their methods of physical examination are full of marvels. Thus more than seventy varieties of pulse are described. The urine is examined with great minuteness in respect to its colour, smell, and clearness, samples passed at many different hours of the day being used. It is also subjected to a kind of auscultation, being beaten with a wooden spatula, and the vessel then quickly applied to the ear. In the case of rich patients, the examination is made more thorough by tasting, a procedure which naturally is made the ground of a special charge.

Mongols, like practitioners of former days in Europe, profess to be able to diagnose and treat all sorts of cases on the strength of an examination of the urine alone. The treatment is largely internal, and their pharmacopœia is mainly composed of vegetable substances. Every year, in September, the students make excursions under the direction of their teachers for the purpose of culling samples, which are dried, classified and catalogued. Aromatic plants such as cinchona and benzoin, play a large part in their therapeutics. Animal and mineral substances are also used, but to a much less extent. The Mongol doctor carries his drugs about with him. Each medicament, dried and triturated, is put into a small leather bag which is properly labelled; some practitioners carry

as many as three hundred of these bags enclosed in a larger one, or in a box with a spoon to measure the doses. Like the ecclesiastic physicians of the Middle Ages, the Llamas are forbidden to practise surgery, although in cases of crushed limbs or other severe injury necessitating amputation, they may direct a butcher how to use a knife. They practise venesection, however, use poultices for the maturation of abscesses, and vigorous massage for the relief of headache and other pains. Recent wounds are dressed with lichen of the steppes or with deer fat. They use counter-irritation by moxas, acupuncture and ignipuncture, and they practise wet-cupping by means of ox-horns.

Preparations of sulphur and lead are used as applications in diseases of the skin, and bathing in hot sulphur springs, in syphilis. Fish's bile is credited with the power of curing cataract. Human bile, and that of the bear and of the hyena, also frequently enter into the composition of their medical preparations. Mongol doctors seek to restore vigour to old men by the internal administration of ram's testicles. 'Organotherapy' is also employed. Thus, the flesh of the sheep is given for vertigo, that of the antelope for diarrhoea, that of the water-rat for nephritis and dropsy, that of the marmot for dysmenorrhœa, that of the beaver for spinal disease and impotence, that of the wolf in diseases of the stomach. They are acquainted with the parasiticide properties of mercury, and use it to destroy the vermin with which their countrymen are generally infected. The most prevalent diseases at Ourga are syphilis and skin affections, but typhus, typhoid, malaria and other fevers are very common. In treating fevers they purge with rhubarb, and when that fails, they give enemata or suppositories, the latter being composed of salt and sugar. They also give nuxvomica sudorifics, and ginger, and juniper is burnt round about the patient. Cholera is treated chiefly by acupuncture under the nails, on the tongue, and around the anus; and as a last resource by burning the pit of the stomach.

Current Topics, Etc.

Indications for Thoracolumbar Sympathectomy in Advanced Essential Hypertension with End Results of Operation in 375 Cases

(Reproduced from *Surgical Newsletter*, W-851, by the American Medical Association and issued by the U.S. Information Service, Calcutta)

HINTON says that while the internist is reluctant to refer early cases of hypertension for operation, which would naturally give more lasting results, he is quite willing to refer advanced cases.

In advanced cases, on which most of the author's experiences were made, the operative mortality is higher than in early cases. It is very important to the surgeon and the internist to have clear-cut indications for accepting or rejecting advanced cases for operation. Death occurring six months post-operatively indicates an unwise selection of patients for thoracolumbar sympathectomy. The only exception to this rule is the case in which papilloedema has produced total blindness, and operation is performed to restore vision. Even when this objective is attained, it must be understood by the patient and his family that life expectancy will not be changed by this procedure.

In a previous report, in which 227 thoracolumbar sympathectomies were reviewed, the author had obtained information about selection of advanced cases for operation. Unfortunately, these criteria were not followed in the 375 cases reviewed here, but since then a system of rules has been adhered to resulting in a higher rejection but a lower mortality.

Four organs are considered in making the selection: the eyes, the cerebrum, the heart and the kidneys, using the rating 0 to plus 4, according to the extent of disease of each organ.

Operation is indicated in all cases in which there is no contra-indication and for patients with persistent hypertension associated with definite though minimal objective changes in any one of the four systems.

Contra-indications to thoracolumbar sympathectomy are: 4 plus renal; 4 plus cardiac in which congestive heart failure is unremitting, or if coronary occlusion occurs within three months; 4 plus cerebral if confusion exists or if a stroke occurs within three months; if there are two 4 pluses other than eyes; if the total plus count equals 11 or more.

If the author had adhered to these rules in consideration of these 375 cases, he would have rejected 25 patients who were accepted for operation and followed over a period of six months. There were 38 deaths, including two suicides after leaving the hospital. If he had followed the rules, 30 of these deaths would have been excluded. On this basis, then, the number of cases accepted for operation should have been 320, and the operative mortality 8, or 2.5 per cent.

Evaluation of end results must take into consideration the extent of the operative procedure. The minimum operation done in about half of the 375 cases included nine thoracic ganglia through the 2nd lumbar ganglion with removal of the greater, lesser and least splanchnic nerves. The operative procedure since then has been much more extensive. It should include the 3rd thoracic ganglion through 3rd lumbar ganglion with all the splanchnic nerves. The more radical the operation the higher the mortality, but also the better end results.

(Hinton, J. W., New York, N.Y.: *The Connecticut State Medical Journal*, 11, 805-807, October 1947. The Author is Clinical Professor of Surgery, Post-Graduate School, Columbia University College of Physicians and Surgeons; Visiting Surgeon, Bellevue Hospital.)

Synthetic Preparation of Vitamin A

(Abstracted from a Report, dated 17th November, 1947, issued by the Trade Commissioner of Netherlands and Netherlands Indies Governments, Bombay)

THE Netherlands chemists, Dr. J. F. Arens and Dr. D. A. van Dorp, belonging to the staff of Organon Ltd., at Oss (Holland), have solved the problem of the artificial preparation of vitamin A after 4 years' research.

Not only does this mean a scientific success of a high order for the Organon Laboratories at Oss but it is, at the same time, of great importance to the medical world and the pharmaceutical and foodstuff industry.

Vitamin A is a vitamin exclusively occurring in the animal kingdom. It is present in milk, butter, yolk, liver and cod-liver oil.

According to the opinion still generally adhered to, it is formed in the animal organism from carotene, a colouring substance, present in almost all greens and yellow fruit. Therefore, this carotene is sometimes called provitamin. Its conversion into vitamin probably takes place in the liver.

In case of lack of this vitamin, a number of deficiency symptoms develop. In the first instance the ability of the eye to adapt itself to seeing with slight light-intensity is reduced. This is called 'night-blindness'. In case of a more serious lack of vitamin A the cornea is affected in the long run, finally causing opaqueness of the cornea. The epithelial cells of other organs, notably the skin, the respiratory and the urinary apparatus, equally show disturbances. This increases the chances of certain infections, while in some species of animals stones have been found in the urinary ducts. Young animals show serious growth disturbances in case vitamin A is lacking. Children and pregnant and nursing women need more vitamin A than adults. In medicine highly concentrated vitamin A preparations are used. These are prepared from certain fish-liver oils, already containing vitamin A in a high concentration.

One may wonder, therefore, whether in man there will ever be a lack of such a substance, the provitamin of which, carotene, occurs so frequently in nature and whether it is necessary that the vitamin itself should be administered to man.

Yet this is really the case.

As a matter of fact, only small quantities of the provitamin are absorbed in the intestines. Hence a large number of cases occur, in which the absorption of carotene is disturbed, thus leading to a lack of vitamin A. Moreover, nurslings and young children have no sufficient vegetable diet to produce a sufficient quantity of vitamin A from the provitamin. Thus it is known, for instance, that during World War I, when Denmark exported the whole of its supply of butter, leaving to the Danes only margarine, lots of children in Denmark showed serious disturbances caused by lack of vitamin A. Therefore, nowadays vitamin A is added to margarine. So the vitaminization of margarine requires vitamin A concentrates which are prepared from fish-liver oils, as mentioned above. Naturally, it is essential that these concentrates be absolutely free from any taste, since otherwise the taste of the margarine would be affected. It is easy to understand that the preparation of these tasteless concentrates from fish-liver oils is not so easy, which is one more reason why it would be important if other routes could be found to obtain vitamin A.

Vitamin A was the first substance the chemical structure of which was elucidated. This was done in 1931 by Karrer *et al.* Afterwards the chemical structures of all other vitamins were elucidated sooner or later after their discovery, but moreover it proved possible to find, for all these other vitamins, methods for building up these substances along chemical routes. In other words, it was not only possible to separate these substances in a pure form from the natural starting materials, but to build them up from the various elements by means of chemical methods.

It is true that in 1937 Kuhn and Morris published a statement that they should be able to prepare a concentrate, which was said to contain 7 per cent vitamin A, synthetically, but the low yield made it appear impossible *a priori* ever to apply this method in practice. Apart from that even the most eminent chemists have never succeeded in confirming this find and since Kuhn and Morris themselves never returned to this subject either, it was doubted whether they had really succeeded in synthesizing vitamin A. Nevertheless, attempts to approach a synthesis of vitamin A were made in many a laboratory all over the world.

For it has proved to be of high importance for the medical world that large quantities of very pure vitamins should be available. Therefore, the vitamin preparations of B₁ and of the other factors of the so-called B-complex, and those of C, D, E and K are almost exclusively prepared along the chemical route, thus being independent of vegetable substances or animal organs in which these vitamins are present. For vitamin A however one is still dependent on the natural materials, the fish-liver concentrates.

The general lack of oils in the world is too well known. Insiders in the vitamin A market are of opinion that at the moment only one-third of the world's need of vitamin A preparations can be covered by fish-liver concentrates. So it is easily understood that the pharmaceutical industry is equally making attempts to prepare vitamin A along chemical routes.

In 1943 the problem and the possibility of synthesizing vitamin A was taken in hand in the Organon Laboratories at Oss by Dr. J. F. Arens and Dr. D. A. van Dorp. What is it that makes the synthesis of vitamin A so extremely difficult? Vitamin A is a complex molecule consisting of a so-called nucleus and a side-chain. The nucleus is a stable substance which is easily obtainable. However, the side-chain is a very frail part of the molecule. When building up the molecule piecemeal one will find that the finished part will collapse, whenever a new piece is added. By building up small parts of the molecule separately and joining them later on, using methods which had never yet been applied in this field of chemistry and are to be considered therefore as entirely original conceptions, Dr. Arens and Dr. van Dorp succeeded in 1944 in obtaining a substance which differed only very little from vitamin A. This was the so-called vitamin A acid, whereas vitamin A itself is an alcohol.

This substance has the same effect on the growth of young rats as vitamin A itself, though it is not converted into vitamin A in the body.

However, the final target was to prepare vitamin A itself. Chemically it is not possible to prepare vitamin A from vitamin A acid, but with the experience obtained so far, the synthesis of vitamin A was once more taken in hand and, after having surmounted numerous difficulties, the investigators succeeded on 8th May, 1947, in building up a substance from which vitamin A could be obtained. It was only one month later that vitamin A itself was prepared.

A substance containing 30-35 per cent vitamin A was obtained.

For those interested in chemical features it may be added that the synthesis of vitamin A was started from beta-ionone, to which a side-chain had to be attached. The first step was to condense beta-ionone with the γ -bromocrotonic ester. Then a methyl group was introduced, applying the Gilman synthesis. From this phase vitamin A acid was prepared by means of a Reformatsky-synthesis. In 1947 it proved possible to prepare the aldehyde instead of the vitamin A acid. The conversion of this aldehyde to vitamin A was known from experiments with vitamin A separated in a crystalline form from fish-liver oils. A control with physical and chemical methods showed that the substance obtained indeed met all requirements put up, while in the animal test an activity such as vitamin A might be expected to show was equally found.

These facts proved that this substance, entirely built up along the chemical route, is fully identical with vitamin A as present in natural sources (e.g. fish-liver oils). So there was no question of having prepared a substance that would be able to substitute vitamin A, but the very substance which is elaborated by nature in quite a different way *via* the vegetable and animal kingdom, had been obtained in a reacting-tube.

As it has been said in the beginning, the final target is to achieve a chemotechnical preparation of vitamin A, a process that is to be considered of high importance on account of the world's lack of sources for the natural vitamin A. Many difficulties will have to be overcome

before this laboratory procedure has been converted into a factory process. It is for the chemotechnical men to act now; the research chemists have laid the indispensable basis for their work.

Post-Penicillin Jaundice

By R. R. HUGHES

(From the *British Medical Journal*, ii, 9th November 1946, p. 685, as abstracted in the *Journal of the American Medical Association*, Vol. 133, 1st February, 1947, p. 352)

HUGHES found that of 121 patients with hepatitis treated in a military hospital in India 36 had had penicillin treatment. He thinks that post-penicillin jaundice is transmitted from patient to patient by means of contaminated syringes. Experiments are described which show that a single intramuscular injection of 1 cc of fluid may lead to contamination of the syringe used. The mechanism by which this contamination occurs is discussed.

Tetraethyl Lead Poisoning

By D. A. K. CASSELLS

and

E. C. DODDS

(From the *British Medical Journal*, ii, 9th November, 1946, p. 681, as abstracted in the *Journal of the American Medical Association*, Vol. 133, 1st February, 1947, p. 352)

TETRAETHYL lead is the active ingredient of ethyl fluid. The regulations governing the cleaning procedure of storage tanks which have contained leaded gasoline were overlooked or disobeyed in some instances, with the result that 25 cases of poisoning occurred, 2 of which were fatal. The earliest symptoms were disturbance of sleep and symptoms referable to the alimentary tract, such as lack of appetite, nausea, vomiting and diarrhoea. Subjective nervous symptoms were irritability, restlessness, nervousness and anxiety. Pallor was not a feature, nor did punctate haemophilia appear. If death does not occur, recovery is usually complete. In the milder cases the treatment is removal from exposure, light exercise in the open air, a normal diet with plenty of fluids and the relief of sleeplessness by a suitable sedative. In severe cases strict nursing supervision is required in view of the impulsive suicidal tendencies.

Outbreak of Industrial Fluorosis in Cattle

By H. H. GREEN

(From the *Proceedings of the Royal Society of Medicine*, Vol. 39, October 1946, p. 795, as abstracted in the *Journal of the American Medical Association*, Vol. 133, 1st February, 1947, p. 353)

DURING the calcining of nonstone, smoke drifts on to neighbouring farms, and on the nearest of these an obscure disease of cattle was reported. Surface contamination of green vegetables is suggested by the author as the source. Samples of urine established a diagnosis by revealing 26 to 69 parts per million of fluorine. Samples of water from the affected farm showed only 0.5 part per million of fluorine, but grass samples within a few hundred yards showed over 2,000 parts per million on the dry matter and the urine of the human family on the farm showed 1.3 to 4.2 parts per million of fluorine, which is above normal and far above the content of the drinking water.

Pseudohæmophilia

By W. PERKINS

(From the *Blood*, Vol. 1, November 1946, p. 497, as abstracted in the *Journal of the American Medical Association*, Vol. 133, 1st February, 1947, p. 349)

PSEUDOHÆMOPHILIA, a condition which is often hereditary, is characterized chiefly by a prolonged bleeding time in the presence of normal platelets is referred to as 'pseudohæmophilia' or 'hereditary hæmorrhagic thrombasthenia'. Perkins presents the history of a patient with this condition, which was transmitted by and occurred only in the male line. The occurrence in the male offspring of the patient's father and of the latter's second wife irrefutably proves this point. The degree of prolongation of the bleeding time varied from day to day and was occasionally normal. Except for transient hypocalcæmia with tetany, no defect in the blood elements or in clot formation was noted. There appears to be a failure of normal capillary constriction following trauma.

The Allergic Pulmonary Reactions of Loeffler's Syndrome

(Abstracted from the *Journal of the American Medical Association*, Vol. 133, 1st February, 1947, p. 325)

LÖEFLER'S syndrome is characterized by frequent changing, pulmonary infiltrations, eosinophilia of the blood and sputum, and a relatively mild clinical course, usually afebrile, in contrast to the pulmonary findings. Frequent x-ray examinations are necessary to understand the changes in the lungs. The syndrome is explained as an allergic response in the lungs to various allergenic substances, including the tubercle bacillus, pollens, *Endamæba histolytica*, the larvæ of *Ascaris lumbricoides*, trichinæ, and nematodes of cutaneous helminthiasis. Fleeting pulmonary consolidations, brucellosis, asthma, amebiasis and trichiniasis have been described. The changes in the few cases examined after death appear to support the allergic explanation, and they may be summarized as bronchitis and pneumonia, lobular and interstitial, with pronounced eosinophilia in the exudation and infiltration coupled with appreciable increase of eosinophils in the blood. Much remains to be learned about the pulmonary reactions of Loeffler's syndrome. The structural alterations in the lungs at various stages of the syndrome have not been described adequately. Perhaps granulomatous processes in other organs, e.g. eosinophilic granuloma of bone, may also be allergic.

More Pitfalls in Diagnosis of Angina

(From the *Lancet*, i, 17th May, 1947, p. 685)

THE fact that cervical arthritis may cause precordial pain has been known for some time, and two American workers report a series of cases in which angina pectoris was closely simulated by ruptured intervertebral disks in the lower cervical spine. Of 30 patients with this lesion, there were 7 in whom the differential diagnosis between ruptured cervical disks and coronary disease had to be carefully considered. These subjects had precordial pain, sometimes radiating to the shoulder and into the arm. In some this was associated with exertion and accompanied by dyspnoea; in others the pain occurred at rest but was so severe that, being accompanied by dyspnoea, it immediately suggested myocardial infarction. Only by careful examination was the possibility of coronary disease excluded. In 3 the diagnosis was confirmed at operation, which revealed a herniated nucleus pulposus compressing the nerve root, and the removal of the herniated nucleus

led to complete relief of pain. In a 4th case the precordial pain occurred only after operation, but was finally relieved by neck retraction.

In establishing the diagnosis the important points are a history of trauma to the neck, and the radiation of the pain which is sometimes rather diffuse. With a ruptured disk, pain which is related by the patient to exertion turns out to be due to strain on the neck or shoulder; another useful guide is a history of repeated attacks of numbness in the fingers. Examination may show wasting of the pectoral muscles, of the biceps, triceps, or small muscles of the hand. The pain may be reproduced by pressure on the head or over the affected nerve root in the brachial plexus, and radiography often reveals characteristic changes in the spine. Where the diagnosis is still in doubt the lack of response to nitrites is a pointer.

Why a ruptured intervertebral disk should cause precordial pain is still unexplained, but it is noteworthy that in one patient in this series pressure on the annulus fibrosus at operation reproduced the precordial pain of which he had been complaining.

Advice on Thunderstorms

(Abstracted from the *Lancet*, i, 17th May, 1947, p. 682)

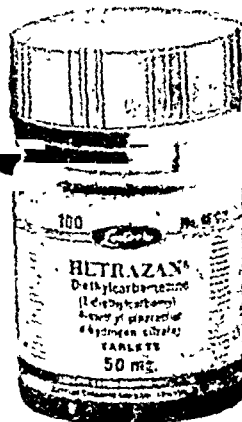
THE *East African Medical Journal* is usefully confident about behaviour in thunderstorms. The best place to be, it affirms, is inside a house with all doors and windows closed and not too near the fireplace; 'to seek further safety in a cellar or clothes cupboard is not necessary'. Lightning is apt to come through an open window with wind and rain. If a chimney is struck, bits of masonry and metal may be blown out into the room and cut an occupant's legs. The neighbourhood of the main switch and meter are also best avoided, since they may be blown up and burnt out if lightning strikes the supply wires; and it is advised that the lead-in wire from the aerial to a radio set should be fitted with a switch so that both may be earthened when thunder is about.

Open windows, doorways, and verandahs are dangerous. If it is impossible to seek sanctuary in a house or a closed motor-car, any solid shed will do, especially if doors and windows can be shut. A shallow shed with one side open is said to be little safer than the open air. Crowds of people and herds of cattle seem to be mildly attractive to lightning. If one is far from home or shelter when the storm breaks the best plan, it seems, is to lie down in a ditch or hollow until it is over; but the writer of the article had no hope that this advice would be widely followed. Single trees, wire fences (which may carry a fatal charge for miles), walls, hedges, river banks, and ponds are dangerous; but apparently the heart of a wood is fairly safe. Finally, the person who is going to be struck is better wet than dry; for wet clothing will short-circuit some of the current.

'A Couple of Aspirins'

(Abstracted from the *Lancet*, i, 17th May, 1947, p. 685)

FOR many years now aspirin has been the domestic panacea. Toxic reactions including gastric hæmorrhage and anaphylactic phenomena may be alarming but are fortunately very uncommon. A recent American report suggests, however, that safety of aspirin for young children has been too readily assumed. Erganian, Forbes and Case have seen, within two years, 13 young patients with symptoms attributed to salicylate intoxication, mostly after aspirin had been given for a 'cold'. All showed a similar pattern of acid-base imbalance which the authors believe to be characteristic of this poisoning in the young. The clinical picture was of a severely toxic, febrile, apathetic, or


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even semicomatose, infant, with increased, deep and pauseless respiration, vomiting, and disinclination for food or drink. The patients were either very pale or cyanosed, and dehydration was pronounced. Spontaneous hæmorrhages in the skin and from the gastrointestinal tract were seen in 2 cases. The urine contained albumin, casts and ketone bodies. Treatment consisted in gastric lavage, subcutaneous glucose-saline, warmth and oxygen; and to counteract the acidosis $M/6$ sodium *r*-lactate was injected in Ringer's solution. In all, except one infant of four and a half months who died from renal failure, the condition improved within two hours.

Erganian and her colleagues find that salicyl compounds in a dosage of about $\frac{1}{2}$ grain per lb. body-weight (in six divided doses) in the twenty-four hours tend to accumulate in the body; and they think that in infants who show no sign of renal failure, diarrhoea, diabetes, or severe infection, the combination of hyperpnoea and listlessness with fever should suggest salicylate intoxication. Aspirin should never be given to infants, and that it should be prescribed for young children only with caution and a watchful eye for signs of over-dosage.

Treatment of Tropical Sprue with Folic Acid

By J. G. MORRISON

and

C. R. ST. JOHNSTON

(Abstracted from the *Lancet*, i, 10th May, 1947, p. 636)

The progress of four cases of tropical sprue treated with synthetic folic acid is described.

Two cases, previously untreated, showed a dramatic improvement both in the blood and in intestinal absorption.

The two other cases, which were of long standing and had long been treated with liver, were improved subjectively, but little or no effect on the blood was observed.

Preservation of Normal Human Plasma in Liquid State

By E. I. LOZNER *et al.*

(From the *Blood*, Vol. 1, November 1946, p. 459, as abstracted in the *Journal of the American Medical Association*, Vol. 133, 1st February, 1947, p. 349)

TRANSFUSION of such plasma is safe and beneficial up to at least three years of storage. The untoward reaction rate following these administrations was significantly less than that following a comparable series of commercially prepared dried plasma. The chemical and physicochemical changes observed in plasma stored in the liquid state at room temperature are of no more clinical significance at the end of three years' storage than at the end of eighteen months. The present National Institute of Health expiration date. Because at the end of six months' storage liquid plasma is devoid of blood coagulation factors, complimentary activity and probably other antibodies; it should not be administered to patients with either hæmorrhagic diatheses or infections and who require these components specifically. Hence it should be used chiefly for its colloid content and should be subject to the same precautions regarding excessive dosage as is human serum albumin.

Against Eponyms

By W. WOLF

(Abstracted from the *Journal of the American Medical Association*, Vol. 133, 1st February, 1947, p. 344)

I SHOULD like to call attention to an article entitled 'Guillain-Barré Syndrome Treated with Neostigmine'

in the 28th December, 1946, issue of the journal, page 1070.

Many of the readers would not bother reading about the Guillain-Barré syndrome since it would be completely foreign to them, while they would be highly interested to know about neostigmine treatment of such a common condition as virus encephalomyelitis. Thus perhaps valuable information would be missed because of personal name reference.

If it is really necessary to cater to the name of the man or men who first described a certain disease for reasons of stimulating people's interest or for reasons of good will, their name might be put in parentheses after the descriptive name rather than the reverse. The writer believes that most medical men should be big enough to give to the profession their description of a new entity without requiring that their names be repeated.

Blood Group Tests of the Newborn

By I. DAVIDSON

(Abstracted from the *Journal of the American Medical Association*, Vol. 133, 1st February, 1947, p. 345)

DR. M. A. HYMAN recommends blood group tests for identification of the newborn child. The suggestion is not practical as it is likely that the tests for factor P and Hr and for subgroups A_1 , A_2 , A_1B , and A_2B would have to be excluded at time of birth in most instances.

Testing serums for factor P are very rare, difficult to obtain and frequently not reliable. Also very rare is testing serum for factor Hr. Tests for factors M and N are best carried out by expertly trained workers. Subgroups of A are frequently not clearly differentiated in the newborn. Subgroup A_2 may be mistaken for O and A_2B for B.

With these reservations, Dr. Hyman's suggestion is worthy of consideration. Tests for the A, B, O and Rh factors would add to the reliability of identification of the newborn infant by footprints. The mother's blood factors should also be determined as part of the pre-natal examination.

Section of the Vagus Nerves to the Stomach in the Treatment of Benign Gastric Ulcer

(Reproduced from *Surgical Newsletter*, W-851, prepared by the American Medical Association and issued by the U.S. Information Service, Calcutta)

HARPER AND DRAGSTEDT say that during the past four years, section of the vagus nerves to the stomach as a method of treatment has been carried out at the University of Chicago in 250 patients with various types of peptic ulcer. The clinical results following this method of treatment have been so satisfactory that it has replaced all other types of surgical treatment for this disease on their service. The side effects on section of the vagus nerves, such as symptoms of delayed gastric emptying and diarrhoea, have proved to be transitory and, on the whole, inconsequential. The operation was performed in 147 patients for duodenal ulcer, in 15 patients with gastrojejunal ulcer and in eight patients with gastric ulcer. The present paper is concerned with the latter group.

The authors stress that all ulcers that were unquestionably benign healed promptly after the total section of the vagus nerves. The reason for this in cases with co-existent duodenal ulcer is fairly evident, as all of the patients in this category secreted large quantities of highly acid gastric juice in the empty stomach. This hypersecretion was eliminated by the vagotomy, and the ulcers healed. The patients with benign gastric ulcer alone, however, without exception displayed a

low volume of night secretion with low free acidity. Although the acid secretion in these patients was reduced after the section of the vagus nerves, it is difficult to understand how such a relatively small change in the acid secretion at such a low concentration could cause prompt healing of a larger ulcer in the stomach.

The fact that gastric ulcers heal after vagotomy, although there may be only a slight change in the concentration of acid in the gastric content, suggests both that other factors than peptic digestion may play a rôle in the formation of these ulcers, and that vagotomy has some effect on these factors. The only known factor in addition to secretion affected by vagotomy is gastric motility. In addition to trauma, hypermotility might conceivably cause the removal of a protective coating of mucus from the surface of the mucosa, exposing the underlying epithelium to irritation.

In regard to the roentgenographic findings, it was observed that the picture conventionally held to distinguish myeloma that of many bones, including the calvarium, riddled by clear-cut punched-out osteolytic defects, represents the exception rather than the rule and applies only to certain cases in which the disease is far advanced. Very often one observes merely some vaguely defined rarefactions in a number of the bones or a single exuberant tumour focus in some one bone without obvious involvement of the skeleton generally. Sometimes skeletal changes may not be apparent at all. As for the calvarium this not infrequently shows numerous punched-out rarefactions, even when roentgenograms show clear-cut and widespread involvement of the rest of the skeleton. In such equivocal or initially obscure cases marrow obtained by sternal puncture is often of great value in establishing the diagnosis.

The average length of survival after the onset of symptoms is not likely to be more than two years, but in occasional patients the course of the disease may be protracted over ten years or more.

Problems in therapy are concerned mainly with palliation, particularly the relief of distressing bone pain and general supportive measures, also the handling of such complications as fractures of bones and compression of the spinal cord.

(Lichtenstein, L., New York, N.Y., and Jaffe, H. L.: *Arch. Path.*, **44**, 207, September 1947. From the Laboratory Division, Hospital for Joint Diseases.)

Visceral Leishmaniasis Complicated by Severe Anæmia—Improvement following Splenectomy

By J. H. BURCHENAL *et al.*

(Abstracted from the *American Journal of Tropical Medicine*, Vol. 27, November 1947, p. 699)

1. THREE patients with leishmaniasis previously reported have now been observed for 23 to 29 months following treatment and so can be presumed cured.

2. A fourth case of leishmaniasis has been discussed which was refractory to all usual dosages of neostibosan, stibnanose, and diamidino stilbene. The anæmia was so severe as to require the transfusion of 51 litres of whole blood during a period of 22 months. The leucopænia was severe and constant. The patient finally recovered following treatment by a combination of very massive dosage of diamidino stilbene and splenectomy. It seems reasonable to assume that the removal by splenectomy of a hitherto inaccessible focus of infection in the tremendously enlarged and infarcted spleen was instrumental in curing the patient.

3. The anæmia and leucopænia disappeared following splenectomy.

4. This last fact leads the authors to postulate that the leucopænia in kala-azar may be caused by the great proliferation of the reticulo-endothelial tissue in the spleen.

5. This report is not to be construed as suggesting the advisability of splenectomy in the usual case of visceral leishmaniasis.

The Occurrence of Water-Soluble Rh Substances in Body Secretions

By J. F. MOHN

and

E. WITEBSKY

(Abstracted from the *New York State Journal of Medicine*, Vol. 48, 1st February, 1948, p. 287)

THE occurrence of Rh substances in saliva could not be determined with any degree of certainty. If present, they were in such low concentrations as to make their demonstration impossible, at least by the methods used in these studies, because of the viscosity of the material.

Rh substances in a water-soluble form are excreted into at least half of gastric juices and into an even larger percentage of amniotic fluids.

Whether this difference in percentage distribution is an actual one or due only to the possible damage to the Rh substances caused by the chemical treatment of gastric juices before they can be examined, cannot be determined at present.

The simple method of purification and concentration of amniotic fluids, as described, seems to allow more definite differentiation between secretors and non-secretors of water-soluble Rh substances.

Hermaphrodites of *Schistosoma mansoni*

By H. VOGEL

(Abstracted from the *Annals of Tropical Medicine and Parasitology*, Vol. 41, September 1947, p. 266)

SECONDARY hermaphrodites of *Schistosoma mansoni* have been described. They show the ordinary characters of males but are provided with an ovary, which, when well developed, contains typical egg-cells. The ovary is situated between the group of testes and the posterior intestinal junction. In some specimens an oviduct and uterus were found in addition to the ovary, but a female genital pore could never be made out with certainty.

Genetically these worms are males. Their transformation into secondary hermaphrodites is favoured by certain species of hosts (guinea-pigs, hamsters, rabbits) and occurs most frequently in the absence of a female partner. Thus guinea-pigs and hamsters infected with male schistosomes only always harboured a higher proportion of hermaphroditic males—10 times in the case of guinea-pigs and 20 times in the case of hamsters—than did similar animals infected with the normal proportion of male and female worms. Males in copula are described, the small embraced partner being a hermaphrodite and the embracing worm a normal male. The possibility is discussed that residence in the host's body, which is essential to sexual development in the female, may likewise stimulate the development of rudimentary female characters in the male.

Phylogenetically, hermaphroditism in schistosomes can be considered as an atavism. By teleological reasoning it might be interpreted as an attempt by the solitary male to compensate for the absence of a female partner.

The sexual abnormality appears to be peculiar to *S. mansoni*, since, under similar conditions, no hermaphrodites were found in *S. japonicum* or *S. haematobium*.

Rudimentary vitelline glands are also described in males of *S. mansoni*. They are situated at both sides of the caecum and occur regardless of ovary development.

Blood Changes in the Aged

By O. OLBRICH

(Abstracted from the *Edinburgh Medical Journal*, Vol. 55, February 1948, p. 100)

1. The red cell population of the aged is distinctly different from that of the young. The quantitative data in regard to erythrocytes, haemoglobin, colour index, total cell volume and mean corpuscular volume do not show any difference between young and old. The mean red cell diameter, however, is distinctly larger in the old, and the scatter as measured by the standard deviation or coefficient of variation is distinctly bigger.

2. The fragility of the red cell population as measured by the osmotic resistance to different concentrations of salt solution is distinctly increased in the old as compared with the young.

3. The blood sedimentation rate is increased in old age and is a function of the plasma proteins, other factors being equal. This is proved by the correlation coefficients and the regression equation; also by experiments involving equal volume exchange of plasma after half an hour's centrifuging. In these experiments:—

- When cells of the young were suspended in plasma of the old, the blood sedimentation rate was increased as in the old.
- When the red cells of the old were suspended in plasma of the young, the blood sedimentation rate was as that of the young.
- When the red cells of an old person whose blood sedimentation rate was normal (between 2 and 10 mm./hr.) were suspended in a plasma of a young person whose blood sedimentation rate was normal, the blood sedimentation rate remained normal.
- When the red cells of an old person were suspended in the plasma of a young person whose blood sedimentation rate was increased, the blood sedimentation rate remained increased.

These results also show that the plasma proteins behave differently in the aged.

4. The total white blood cells are present in equal numbers in the blood of the old and the young, but the differential count shows an entirely different behaviour as regards the number of lobes. The cells, which contain more than 3 lobes, are increased in number in relation to the total (100 per cent); and at the same time the cytoplasm in the multilobulated cells contains fewer granules, in such a relation that the more lobes the nucleus has, the less granules the cytoplasm contains. Cells were even seen containing more than 5 lobes and containing scanty or no granules in the cytoplasm.

5. The non-protein nitrogen shows a distinct increase with advancing years, but not beyond the 'normal' range.

6. From all the data with regard to the red and white cell population of the aged, we might venture the hypothesis—in view of their maintained numerical quantity but different qualitative behaviour—that the bone marrow produces in one time-unit a lesser amount of red cells and leucocytes. This means that the rate of production in the aged is diminished. At the

same time, however, the rate of destruction is also diminished and a cell population is maintained probably for a longer time in the older person, but apparently of a different quality.

7. The nutritional condition of the subjects has been investigated and it has been found that protein, fat, carbohydrate intake and total calorie intake are approximately the same as that of the general population, taking body weight into account.

Vagotomy in the Treatment of Peptic Ulcer

By C. F. W. ILLINGWORTH

and

A. W. KAY

(Abstracted from the *Edinburgh Medical Journal*, Vol. 54, October 1947, p. 540)

In the treatment of peptic ulcer, whether by medical measures or conservative surgical operation, there are two main objectives—to reduce the acidity of the gastric juice and to put the ulcerated part at rest.

Since vagus stimulation is known to bring about the secretion of the 'appetite' juice and to enhance the motor activity of the stomach, it seemed reasonable to suppose that these objectives might be attained by division of the vagus nerves.

The operation of vagotomy was introduced by Exner in 1914 for the relief of pain in the gastric crises of tabes and only recently has it been applied in the treatment of peptic ulcer. The object of the present paper is to report the results in a small series in which the denervation was carried out by the abdominal approach.

Clinical cases.—Since the observations were of an experimental character, it seemed proper to restrict them to a small series of 6 cases. The patients were carefully selected. All had duodenal ulcer; in one there was also a gastric ulcer. All were men of similar ages, all gave a long history of severe indigestion which had resisted or relapsed after one or more periods of careful medical treatment in hospital. All were suffering, at the time of operation, from a severe and prolonged attack.

After operation there was a striking change, and gastriograms in all cases showed almost complete immobility, with only occasional slight alterations of tone to disturb the calm.

The effect of vagotomy on the acid secretion, on the other hand, was slight. In 3 cases there appeared to be some diminution in the volume of juice secreted, but the acid level was practically unchanged. This is in accord with expectation since the hormonal stimulation of acid remains unaffected.

Results.—The immediate results appeared satisfactory and all 6 patients experienced complete relief of the pain and indigestion from which they had suffered prior to operation. Even making full allowance for the tendency of peptic ulcer to undergo spontaneous remission it did seem that the vagotomy had been effective, and this appears to be confirmed by the fact that 5 of the patients remained symptom-free for eighteen months or more.

Unfortunately the relief did not prove permanent. One patient, the case with gastric as well as duodenal ulcer, suffered a relapse within three months; further operation showed that the gastric ulcer had penetrated the pancreas. Gastrectomy was performed and he has remained well since. Two others have required gastrectomy, having relapsed after eighteen months and two years respectively. A fourth patient relapsed after eighteen months but not severely. The remaining two continue symptom-free after three years.

Motility records show that in each case the return of symptoms was preceded by return of motor activity

and a positive response to prostigmine. These findings suggest that the recurrence was due to regeneration of the cut nerves. In two cases this was confirmed by microscopic examination after gastrectomy.

Effects of Heparin on the Action of the Venoms of Some American Viperine Snakes

By M. L. AHUJA *et al.*

(Abstracted from the *Indian Journal of Medical Research*, Vol. 35, July 1947, p. 227)

1. EXPERIMENTAL evidence is presented to show that heparin effectively neutralizes, *in vitro*, the blood coagulant action of the venoms of viperine snakes: *B. alternatus*, *B. jararacussu*, *B. atrox*, *B. cotiara*, *B. neuwiedii* and *Crotalus terrificus*.

2. Heparin counteracts some of the toxic effects of the venoms of *B. alternatus*, *B. jararacussu*, *B. atrox* and *B. cotiara* in experimental animals.

3. The trial of heparin as a therapeutic agent in the bites by the above-mentioned viperine snakes is suggested.

Heart-beats

By J. E. HILL

(Abstracted from the *Current Science*, Vol. 16, October 1947, p. 305)

ACCORDING to the average person's heart-beats about 72 times a minute, 4,300 times an hour, and more than 2,500,000 times in a life-time of 70 years. While you are reading this, each minute the heart pumps about 10 quarts of blood, doing work at a rate of about 200 foot-pounds per minute. If you are in good physical condition and run quickly up a flight of stairs, your heart may work three times as hard.

The pulse rate varies greatly in different mammals. When a mouse is resting, its pulse is about 700, ten times as fast as man's. A cat's heart beats about 120 per minute, a dog's 85 to 125, while a horse's or cow's heart beats only 35 to 45 times a minute. The heart beats more rapidly in a young mammal than in an older one. Even in adults of the same species a small individual has a faster heart-beat than a large individual. A toy terrier, for instance, may have a pulse more than half again as fast as a St. Bernard's. From this, the conclusion may be drawn that the heart rate in mammals generally decreases with an increase in size.

This is because a small mammal lives at a high speed. A mouse's metabolic rate, measured by its consumption of oxygen per unit of weight, is about 20 times that of a man. A small dog may need, for its size, twice as much food as a large dog. The rapid loss of heat by radiation from a small body requires the 'fires' of life to blaze high continually.

Some of the extra circulation necessitated by these factors may be provided, in part, by relatively large hearts. The normal human heart is about one-two-hundredth of the weight of the body. The heart of a small bat may be relatively three times as large. Mammals that lead a very active life, as diggers or swift runners, may have disproportionately large hearts. That of a deer, a badger, a wolf, or a weasel may be one-hundredth of its weight. In contrast, hearts of sedentary domestic animals or secretive rodents are only about one-half or one-third as large. A jack rabbit's heart is almost three times as big as that of a domestic rabbit weighing the same amount; and when it is resting, it pumps about the same amount

of blood but at a rate only one-third as fast. When the jack rabbit must run for its life, its heart can speed up and pump four times as much as while resting.

There is a relation between the speed of the heart-beat and the life-span of an animal. The mouse, with a pulse rate of 700, lives only about two years; its heart performs a total of some 700,000,000 beats. A cat or dog lives through about the same number of heart-beats, and an elephant may live through 1,000,000,000. Some of the smaller bats, with the fastest heart-beat of any mammal, live eight years or more. If they hibernate, as they do in the cold north, the heart-beat drops from 700 or more to only 30 a minute. Allowing for this decrease in activity, such bats have a heart-life of some 2,000,000,000 beats.

The Transmission of *Wuchereria bancrofti* by *Anopheles darlingi* in the American Tropics

By G. GIGLIOLI

(Abstracted from the *American Journal of Tropical Medicine*, Vol. 28, January 1948, p. 71)

THE transmission of *Wuchereria bancrofti* in British Guiana is studied in relation to the infectibility, the house-frequenting habits and the biting habits of the local mosquitoes.

Mosquitoes were collected from two representative localities: (a) a non-sewered suburb of George Town, highly infected with filariasis, in which *C. fatigans* is the prevailing mosquito; (b) a coastal sugar estate village, with a relatively low filarial incidence and *A. darlingi* as the dominant mosquito. The technique adopted for dissection is described, as this is an important point when comparative work is being undertaken. In the aggregate, 19,407 mosquitoes were dissected. Dissections were made on samples of mosquitoes collected from houses at random and from houses where there was known to be filariasis. The results of immediate dissections and of those made on mosquitoes kept alive for 7 to 12 days after capture are compared.

In both localities the relative incidence of natural infection in *A. darlingi* was very considerably higher than in *C. fatigans*.

A series of comparative infectibility experiments were undertaken with *C. fatigans* and *A. darlingi*, *C. fatigans* and *Aedes aegypti*, and *A. darlingi* and *Aedes aegypti*.

A. darlingi appears to be just as suitable a host for *Wuchereria* as *C. fatigans*, its classical vector; the specific anthropophilic feeding habits which cause *A. darlingi* to be the most effective malaria carrier of Equatorial America obviously also make the mosquito a particularly dangerous vector of filariasis.

Attempts to infect *Aedes aegypti* experimentally failed entirely, the negative rôle of this species in the transmission of *Wuchereria* being further confirmed.

Treatment of Herpes Zoster with Cobra Venom and Sulphanilamide

By M. G. TAN *et al.*

(Abstracted from the *Journal of the Philippine Medical Association*, Vol. 23, December 1947, p. 693)

THE result of our treatment of five cases of herpes zoster seen in private practice with cobra venom and sulphanilamide in combination is presented as a preliminary study. It is to relieve the patients from the troublesome subjective symptoms of the disease

PRESSURE DRESSING FOR A SCALD

AUGUST 22nd, 1947. Scalded at work. Next day, attended hospital with a large blister of inner aspect R. ankle (Fig. 1).

Treatment. Scalded area dressed with Jelonet (tulle gras), Viscopaste bandage applied from toes to knee. Pressure pad of cotton-wool applied over scalded area. The whole leg firmly bandaged with Elastocrepe, with especially firm pressure over the scalded area (Fig. 2).



Fig 1

7th October, 1947. When bandages were removed, wound soundly healed (Fig. 3).

Comment. Firm pressure dressing afforded immediate comfort, permitting ambulatory treatment and continuation at work.

These details and illustrations are of an actual case. T. J. Smith & Nephew, Ltd, of Hull, England, manufacturers of Elastoplast, Elastocrepe, Jelonet and Viscopaste, publish this instance—typical of many—in which their products have been used with success.



Fig 3



Fig. 2

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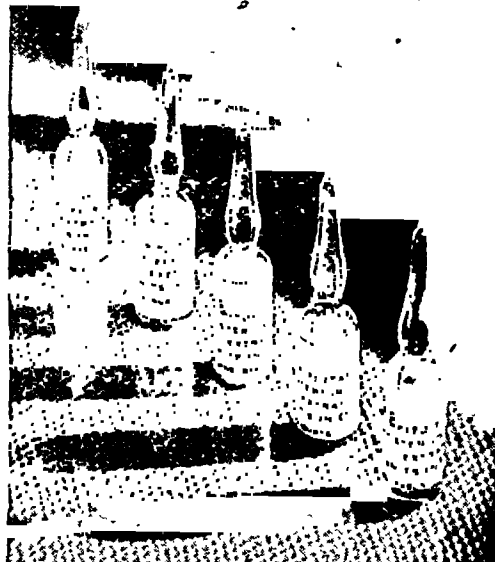


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that cobra venom was thought of as a comforting measure to tide patients over a period of distress. Because sulphanilamide had been reported with success in the treatment of some viral diseases like trachoma, lymphogranuloma venereum, and smallpox, the witness believed that it would similarly be effective on herpes zoster whose aetiology is supposed to be a specific filterable virus.

All the 5 patients who received this treatment were benefited. The writers did not encounter any unfavourable reaction either from the cobra venom injection or from the sulphanilamide administration. After an average of 3 cobra venom injections, relief from neuralgic pain was noted, and the herpetic eruption completely disappeared in four of our cases. Five injections were necessary in one who had post-herpetic syndrome.

Although this method of treatment is not expected to replace other forms through which successful results have been claimed, it deserves a therapeutic trial. The writers are aware that an accurate appraisal of the value of this form of therapy requires a further controlled investigation in a much larger series of similar cases.

The course of treatment in the five cases under study consisted of three doses of cobra venom in one female and two male adults, five doses in another male adult who had post-zonal syndrome, and three doses (1 cc. each of 1 : 10,000, 1 : 10,000 and 1 : 5,000 dilution) in the girl patient. The sites of injection were selected alternately from the deltoid region to the supero-lateral quadrant of the buttocks.

Effect of Copper Sulphate on *Vibrio cholerae*

By A. HALAWANI

and

A. A. OMAR

(Abstracted from the *Journal of the Royal Egyptian Medical Association*, Vol. 30, November 1947, p. 517)

THE results of the authors' experiments show clearly that copper sulphate in dilutions ranging from 20 to 45 parts per million have a definite lethal effect on heavy emulsions ranging from 10 to 1,000 million organisms per ml. It is almost certain that such density of organism never occurs in nature if canals become contaminated. Further, it seems that the concentration of copper sulphate required to kill all the vibrios present depends on the density of these organisms in water as shown in the 3rd and 4th experiment; a dilution of 20 parts per million was sufficient to sterilize an emulsion containing 10 million organisms in each cubic centimetre of Nile water. Chemical estimation of copper in water has shown that it is almost completely precipitated after 24 hours and that out of 30 parts per million only 7 parts remained detectable after 75 hours. Copper in such dilutions is known not to be harmful to men, animals or plants.

The authors believe that copper sulphate has its place in the prevention of cholera in Egypt as it is used in this country in the eradication of snails in water canals.

The Defence of Egypt against Cholera in the Past, Present and Future

By M. K. BEY

(Abstracted from the *Journal of the Royal Egyptian Medical Association*, Vol. 30, December 1947, p. 608)

The Partition of the Punjab Province between Hindusthan and Pakistan was the direct cause of the introduction of cholera into Egypt.

On the 15th August, 1947, India was given dominion status and was divided into two states, Hindusthan

and Pakistan. The Punjab province was divided between the two countries. Moslems began to emigrate from the Hindusthan section and Hindus from the Pakistan section. Five millions emigrated under severe conditions. They were massacred, they had to travel on foot carrying their children, old people and those who were ill as well as their luggage. Sanitary measures were non-existent on the roads. This happened at a time favourable for outbreaks of cholera. A severe epidemic broke out on or about 31st August. Photographs and alarming news were published and broadcast. It was stated that on one occasion 100 cases of cholera were found among the passengers of one train.

In addition British troops began their withdrawal from India on the 15th August. The troops used the Suez Canal area as a station on their way to the British Isles. This was a quarantine measure to protect Britain from possible epidemics brought by the troops from India.

The Suez Canal Area was directly connected with India by sea and by aerial transport. The British military authorities used unauthorized inland ports along the Suez Canal where no quarantine measures were taken. Several military aerodromes were used for receiving aircraft coming from India. This procedure is illegal according to the International Sanitary Convention for Aerial Navigation which enacts that the first landing of an aircraft coming from abroad must be in an aerodrome where there is a local sanitary authority.

In these circumstances the Egyptian Ministry of Health ought to have applied article 24 of the International Sanitary Convention but an official statement was published in the local press (which I hope is not true) to the effect that no country took measures when cholera broke out between the emigrants of the Punjab, and Egypt acted in the same way. Egypt, however, is the first country in direct aerial communication with India where passengers may pass several days and mix with the population. Military personnel landing in the canal zone aerodromes pass at least 15 days in Egypt as quarantine measure for the benefit of the British Isles. Aerodromes in Iran and Basra are situated in isolated places away from towns and aircraft stay only a few hours for fuel. Even if passengers pass the night there, they sleep in the aerodromes and have no chance to mix with the population.

The quarantine authorities have to be alert to international events and have to take immediate measures to prevent the catastrophe before it occurs. There are some examples:

1. In 1865 when cholera broke out in Egypt and spread to Europe, the Health Committee of New York secured extraordinary powers to prevent cholera. New York was cleaned thoroughly. Thirty-six ships were put under quarantine on arrival from Europe. This was executed before the end of 1865. The first cases of cholera occurred in the U.S.A. about the middle of 1866.

2. When the first cases of cholera were declared in Egypt in the present epidemic, Syria and Lebanon decided immediately to put all persons arriving from Egypt under quarantine for 5 days and have their stools bacteriologically examined. This is the correct procedure that ought to have been adopted by Egypt in the first week of August when a severe epidemic of cholera broke out amongst the emigrants from the Punjab. This procedure was formerly discussed and adopted by the Arab League. It is for this reason that the administration of the Arab League on the writer's suggestion sent telegrams of congratulation to the health authorities in these countries for their prompt action adopting the measures which ensured the safety of their countries.

3. The Government of Iran stopped all aerial transport from Egypt. This measure is not mentioned in the Sanitary Convention. Every country in virtue of

its sovereign rights can adopt any measure it considers necessary to ensure its safety even if it is contrary to the convention. If the measure adopted is injurious to the interests of an individual or a concern outside the country, they are entitled to damages. Very rarely such damages are claimed.

4. The Sanitary Conventions do not sanction measures against goods as cotton or against letters or journals. However, certain countries prohibited shipment of Egyptian cotton and others prohibited letters and journals from Egypt. The transmission of cholera by such means is practically impossible.

The measure adopted by any one country reflect the mental attitude of its sanitary authorities and the standard of general sanitation of the population.

A CASE OF CHOLERA WAS SUSPECTED AT KOREIN ON THE 22ND SEPTEMBER, 1947

When a private practitioner suspects a case of cholera among his patients it is probable that the disease existed in the country for several days or weeks before. H. E. Dr. Samy Bey Shawkat, a former minister of Social Affairs and Public Health in Iraq, on the basis of his personal experience of 3 epidemics of cholera there, stated in Cairo on the 18th October, 1947, that cholera was probably introduced into Egypt 2 to 3 weeks before that date.

Dr. Dimitri Salama, a private practitioner in Faqus, sent a patient who was brought to his clinic from Korein to the fever hospital with the diagnosis of cholera at 9-30 a.m. on the 22nd September, 1947. Dr. Salama, a former student and assistant of mine, is a capable and distinguished medical man.

It was officially announced on the 26th September, 1947, that the diagnosis was confirmed bacteriologically.

Cases suspected to be cholera were reported independently on the same day at about midday at Mostorod near Cairo by Dr. Moh. Kamal Abdel Hadi el Gogary. He qualified only a few months earlier and in spite of the opposition and ridicule he received from his subordinates and chiefs he insisted on his diagnosis which proved to be correct.

A commission of investigation ought to have been formed at once and charged with the duty of discovering how cholera entered Egypt, in order to prevent a repetition of the disaster in the present and in the future. Those responsible for the introduction of the disease should have been identified and properly dealt with.

The advent of cholera in 1831 was the direct cause of the institution of a committee of the foreign consuls in Alexandria to supervise the health conditions of Egypt. Later, this committee developed into the Quarantine Health Board. Egypt was not able to abolish this international organization except after a considerable effort in 1939.

Diet in Typhoid Fever

By R. N. CHAUDHURI

(Abstracted from the *Journal of the Indian Medical Association*, Vol. 18, November 1948, p. 43)

To understand the rationale of dietetic treatment we must remember that typhoid like other acute fevers causes an increase of 7 per cent in metabolic rate for each rise of 1°F. in body temperature. This increase in the metabolic rate during the height of fever may be as much as 40 per cent or more. There is consequently increased combustion of body stores and tissues with increased tissue protein destruction which may be as much as three times the 'wear and tear' of health. There is increased nitrogen excretion causing a negative nitrogen balance. Protein destruction is also reflected in the changes in the plasma proteins. In

typhoid generally there is some reduction of the total protein due to reduction of the albumin fraction, while the globulin remains practically unchanged or shows a slight increase during recovery. The degree of hypoproteinaemia and hypoalbuminaemia depends on the severity of illness; it is noticeable even in the first week and becomes most marked about the third week of the disease. This is further aggravated if the diet is restricted but is usually not altogether prevented by giving even fairly good food. With recovery, however, the normal level is restored.

Carbohydrate metabolism in typhoid is also influenced in that the liver becomes glycogen-poor and the stores of glycogen elsewhere are exhausted. With a view to find out how glucose is absorbed and tolerated in this disease we did glucose tolerance tests in a series of cases during the height of illness. The results show that glucose by mouth is readily absorbed. In some cases the curve was normal but in others it was abnormally high indicating impairment of the sugar tolerance. In fact, in a few cases definite diabetic type of curve was noted with passage of sugar in the urine but the tests repeated during convalescence were normal. These findings are comparable to the results of glucose tolerance tests carried out in starvation cases during the Bengal famine. Fat metabolism does not differ from that in health except that when on a starvation diet the patient is forced to draw on his stores of body fat.

To sum up in the background of typhoid fever there proceeds rather excessive protein destruction which often goes unrecognized and untreated. A prolonged period of protein deficiency leads to a negative nitrogen balance. To a certain extent this is inevitable but its effects can be minimized by giving diets of high calorie value and high protein content. The importance of keeping a high protein level lies in the fact that it enables the body to better resist the infection and shorten the convalescence. The sugar tolerance is apt to be impaired apparently due to the effect of starvation and infection.

GENERAL PRINCIPLES

Based on the above findings, the general principles in feeding a typhoid patient may be enumerated as follows:—

1. The diet must have a high calorie value to maintain the metabolic equilibrium, about 40 calories per kg. body weight up to 3,000 calories for an average patient. The actual amount can be determined only by the patient's individual needs; his likes and dislikes must also be considered. The clinical guides are the weight of the patient and the state of his appetite. The latter is not always a useful guide, and in the early stages it may be difficult to make him take sufficient food, but effort must be made to give at least 2,000 calories. Much can be done by persuasion, by keeping the mouth scrupulously clean and by avoiding a monotonous diet. Later, patients take food more readily.

2. A liberal amount of protein must be provided—1 to 1½ gm. per kg.—about 60 to 90 gm. should suffice. Proteins build new tissues, repair exhausted tissues and also supply some body heat.

3. Carbohydrate should furnish the major part of the diet. This will spare protein destruction, prevent ketosis and also replenish the glycogenic store of the liver. About 300 to 400 grammes are given.

4. A diet with sufficient fat may be taken with benefit. It may be almost the same proportion as protein, i.e. 1 to 1½ gm. per kg. It supplies 1/4 to 1/3 of the total calories.

5. Small frequent feeds every two or three hours should be adopted.

6. Ample fluid intake should be ensured, about 5 pints a day.

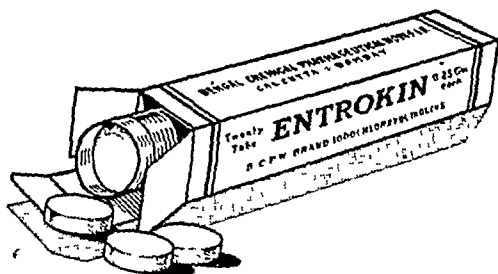
7. During convalescence increased appetite is common, and it is best to proceed a little slowly and not

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to permit food intake beyond the patient's digestive powers.

Next we come to practical considerations in feeding typhoid patients. Say, we have an adult (typhoid case) weighing 60 kilo. wt. (most patients weigh 50 kg.). An adequate total caloric requirement would be $60 \times 40 = 2,400$.

OBJECTIONS

Questions arise:—

1. Can the patient digest all the food? (During fever digestive functions are apt to be depressed.)
2. Is the food absorbed properly?
3. Is there any risk of solids causing more danger to the small intestine which is ulcerated?
4. Can the diet cause further rise of temperature?
5. With liberal feeding will the waste products of protein add to toxæmia?
6. Are relapses more common when a liberal diet is given?

These were the objections raised by older physicians against the procedure of liberal feeding of typhoid patients.

It is not here possible to go into details but I may say that Von Hosslin, Du Bois and others who carried out an elaborate study of metabolic process in typhoid fever by quantitative analysis of diet on one side and examination of urine and stool on the other concluded that protein and carbohydrates are absorbed as well as in normals throughout the illness and large quantity of fat can also be absorbed but percentage of absorption is slightly lower especially in the earlier part of illness. Food reaches the small intestine in a practically liquid form and does not cause any mechanical damage to the gut. No specific dynamic action from liberal diet was observed in causing higher rise of temperature nor was the relapse rate significantly higher as compared with controls. The fear that waste products of dietary proteins may add to toxæmia appears to be too theoretical.

SELECTION OF FOOD

In selection of diet we have to consider the patient's own choice, and digestibility, energy value and the palatability of food as well as his general condition—whether he can masticate and take solids or not. All patients cannot be fed alike by rule of thumb—their preferences and idiosyncrasies must be considered. Sometimes it is difficult to feed a typhoid patient, but he should be given as much nutritious food as possible. Careful attention is to be paid to detail and monotony avoided by varieties. The quality and quantity of food may have to be modified according to special symptoms or complications.

Certain articles of diet are referred to below from which selections may be made:—

1. *Milk* is the main basis of diet and should be given in adequate quantity, 1 to 1½ seers daily. It may be diluted with water, citrated or peptonized. It has valuable nutritive qualities and also provides a vehicle for the administration of other foods, e.g. sugar, egg, cream, bread, gruel, etc. A seer and a half yields about 1,000 calories. If milk is distasteful it may be flavoured with tea or coffee. Proprietary powder preparations such as Klim, Nespray, Nestle's malted milk, Horlicks or Mellin's food may be used as a substitute for a milk feed or mixed with the milk to taste. A feed containing 2 oz. milk powder, ½ oz. sugar in 8 oz. water would give 360 calories; while a cup of milk (8 oz.) with ½ oz. sugar supplies 220 calories.

2. *Sugar* is used to sweeten the feeds and supply calories. It can be given in liberal amounts. Four ounces yield about 500 calories. As an alternative to cane sugar glucose, dextrimaltose or lactose may be

used. Lactose is less sweet and does not cause much fermentation.

3. *Barley, arrowroot or sago* may be added to milk and sugar. Half an ounce yields 50 calories.

4. *Bread* may be given with milk as 'typhoid bread' or in thin slices with or without butter.

Potato (mashed) may be given with little butter or mixed with vegetable or fish broth. *Rice* or *chura* may be used as gruel with milk or may be taken with fish or potato. Two ounces of any of these yield about 150 calories.

5. *Eggs* are a good source of protein and fat, and can be given lightly boiled or poached or given mixed with milk and sugar and as egg-flip or custard. One egg supplies about 80 calories.

6. *Fish* can be given mixed with smashed potato or in the form of broth after separating the bones. Lean fish like *Singhi* or *Magur* is preferable and convenient for this purpose. Four ounces supply about 90 calories. *Chicken soup* is a good change and is often liked by patients used to it, but is better withheld if there is looseness of bowels.

7. *Butter* (½ oz. = 108 calories) and *cream* (1 oz. of 20 per cent cream = 60 calories) can be used to supply extra fat and calories especially if there is no diarrhoea.

8. *Fruit juice* (orange, sweet lime, pomegranate, etc.) serves as a useful and palatable drink to which sugar and salt are added. Cream may be given with fruit juice to increase the caloric value.

9. *Salt*. Some salt should be given to prevent hypochloremia. It can be added to fruit juice, drinks, potato and soup or broth.

Feeds are given at intervals of 2 hours, 9 feeds being given daily.

If two hourly feeds are not possible the patient may be fed three hourly. Feeds nos. 1, 2, 4, 6, 7 and 9 are given at 6 and 9 a.m., 12, 3, 6 and 9 p.m. taking care to increase the caloric value of each feed as much as possible.

The food has to be varied and the quality and quantity modified according to the individual case. Some water is usually given after each feed and also in between, the total fluid intake being 5 pints.

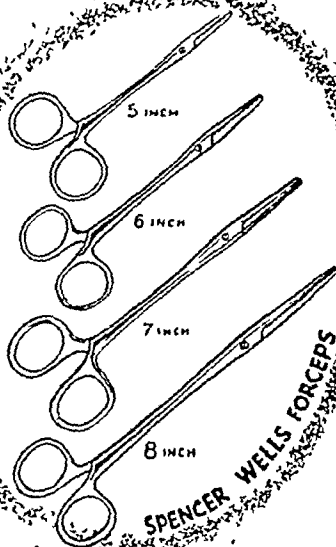
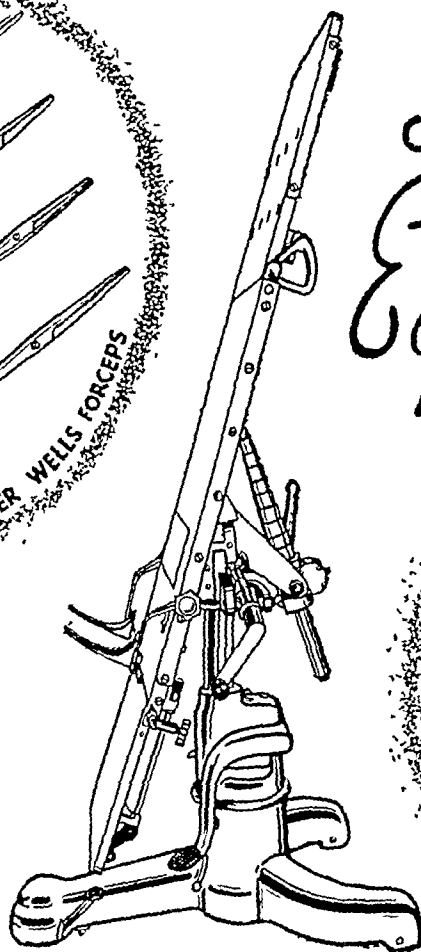
DIET IN PRESENCE OF COMPLICATIONS

If there is marked distension (slight tympanitis is a common feature in typhoid and is no contra-indication to liberal diet) or if the bowels tend to be loose the diet has to be adjusted: fat, fruit juice, soup and sugar are reduced or modified, or temporarily withheld according to the severity of the case. Milk may be given in the form of lactic acid milk, or skimmed milk, or butter milk or whey. Lactose may replace sugar or glucose to avoid fermentation. Proprietary preparations like Eledon on Mellin's food may be used, while arrowroot is a well-tolerated carbohydrate. If such modification or restriction of diet amounts to reduction of protein intake predigested proteins should be given, for which proprietary preparations like Biotol, Pronutrin or Amigen are recommended. An ounce of these yields about 30 gm. of protein (120 calories). Extra vitamins especially of B group and C should also be given. If the patient is dehydrated 5 per cent glucose saline (250 to 500 cc.) is indicated along with adequate supply of vitamins. It may be necessary to resort to plasma transfusion to meet the needs of the patient during the critical stage when the patient is so ill that he cannot take adequate food and fluids by mouth and there is apprehension of circulatory failure. About 500 cc. may be given by drip method. It provides protein, combats dehydration and medical shock with surprisingly remarkable results. Nasal feeds should also be given until the patient can take them by mouth. Nasal feeds are given six or eight hourly, two or three each consisting of milk, 12 oz. or so, sugar 2 oz. and an egg if possible are given while

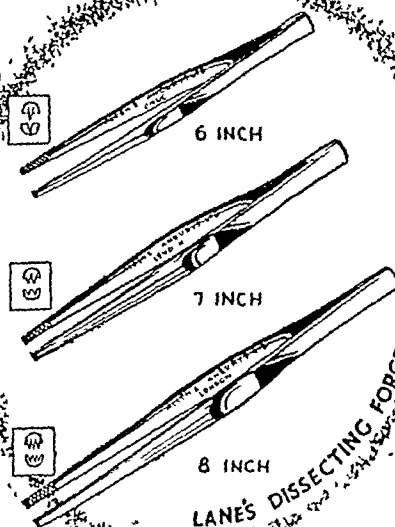
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Yellow Fever Vaccine Inactivation Studies

By H. W. BURRUSS

and

M. V. HARGETTE

(Abstracted from the *Public Health Reports*, Vol. 62, 27th June, 1947, p. 940)

Forty-nine different yellow fever vaccines were subjected to a variety of environments to determine what effect these environments might exert on the potency of the vaccines. The experiments are presented in seven studies.

Vaccine desiccated at 'room temperature' is as stable as vaccine desiccated at 38°C. to 40°C.

Each of 20 desiccated vaccines held in cold storage (—9°C. to —32°C.) for three years was found to be adequately potent for use at the termination of the storage period. Vaccine stored at —5°C. to —7°C. and warmer showed considerable loss of active virus during a storage period of 2 years. It is recommended that desiccated vaccine be stored at —20°C. to —25°C. Electric ice-cream storage cabinets and commercial cold storage warehouses commonly afford such storage.

Desiccated vaccine may still be adequately potent for use after an exposure of several weeks to a tropical temperature. Exposed at 37°C., an average of 90 per cent of virus was lost in two weeks and 99 per cent in 8 weeks; active virus was present after 104 weeks. Each of eight different vaccines showed a significant increase in titre when exposed 7 or 8 hours at 25°C. to 37°C. Each of these same eight lots still contained adequate virus of immunization after 7 or 8 hours' exposure at 80°C.; an exposure of 7 or 8 hours at 110°C. and 100°C., respectively, was required to inactivate all virus.

Each of four vaccines diluted 1 : 1 with physiologic saline at 37°C. and held for 2 hours at that temperature showed a significant elevation in titre. Vaccine diluted 1 : 1 to 1 : 100 with saline remained adequately potent for from 620 hours when held at 37°C. Some dilutions showed active virus still present after 48 hours.

The inherent character of the 17D virus employed in vaccine manufacture is an important factor in determining the stability of the product. Only substrains of known good characteristics should be used for seed virus, and stabilization of the virus should be insured by employment of the seed-lot system.

One millilitre of vaccine of ordinary good quality is ample to successfully vaccinate 200 persons when the vaccine is diluted 1 : 100 and administered in a volume of 0.50 ml. per recipient.

Relative to vaccine administration it is recommended: (a) that only preparations be employed which comply with the minimum requirements set up by the Biologics Control Laboratory, (b) that vaccine be stored at —20°C. or colder until time of use, (c) that neither desiccated nor diluted preparations be unnecessarily exposed to heat or light, (d) that 1 : 1 and 1 : 10 suspensions be used within 1 hour of preparation and 1 : 100 suspensions within 10 minutes, and (e) that if vaccine of questionable potency must be used, 10 to 20 times the usual quantity be administered.

Reviews

OCULAR SIGNS IN SLIT-LAMP MICROSCOPY.

By James Hamilton Doggart, M.A., M.D. (Cantab.), F.R.C.S. (Eng.). 1949. Henry Kimpton, London. Pp. xiii plus 112 and 93 illustrations with 85 in colour. Price, 21s.

This is an essentially practical book on the clinical phenomena which can be observed with the slit-lamp and corneal microscope. Its chief feature is the

magnificence of its 93 illustrations of which 85 are in colour. The book contains all that the D.O.M.S. student requires to know about clinical slit-lamp microscopy, in spite of the fact that there are only 98 pages of subject-matter. The printing, paper and general standard of excellence make the price of 21 shillings seem reasonable. Mr. Doggart has written a very readable and very helpful book and it is to be thoroughly recommended.

E. J. S.

THE PHYSIOLOGY OF THE EYE.—By Hugh Davson, D.Sc. (Lond.). 1949. J. and A. Churchill Ltd., London. Pp. xi plus 451 with 301 illustrations. Price, 32s.

Most standard textbooks of general physiology contain comparatively little on ocular physiology so that the post-graduate student preparing for the ocular physiology papers in the D.O.M.S. uses Duke-Elder's monumental 'Vol. I'. Before reading this it is of great advantage to know something of the subject. Mr. Davson's book covers the same field in some 319 pages and is ideal for a first reading in the subject. The matter is presented in a rather concentrated form so that the student will be wise subsequently to read his 'Vol. I'. Later on Mr. Davson's book will be ideal for revision. The author has had much experience in teaching physiology and physiological optics for the Diploma in Ophthalmology in London so that his book covers all that is required. The printing, paper and illustrations are excellent and the style is clear and easy to read. The last 115 pages of the book summarize physiological optics. This book supplies a much-felt want and will be a boon to D.O.M.S. students.

E. J. S.

DOCUMENTA OPHTHALMOLOGICA—ADVANCES IN OPHTHALMOLOGY.—By F. P. Fischer (Utrecht), A. J. Schaeffer (Los Angeles), and Arnold Sorsby (London). Vol. II. 1949. Pp. v plus 461 with illustrations. 'S-Gravenhage: Uitgeverij Dr. W. Junk.

This is a collection of eight papers. G. Wald of New York writes an obituary notice in English on Professor Selig Hecht. A. v. Tschernak-Seysenegg of Prague writes on Simultaneous Contrast in German with a short summary in English. Next W. Bronkhorst of Bilthoven, J. Ten Doesschate and F. F. Fischer of Utrecht discuss the Physiological Optics of the Visualization of X-ray Pictures in English with a summary in French. R. Weekers and P. Roussell of Liege describe the Measurement of the Frequency of Fusion and its clinical application in French with an English summary. J. Ten Doesschate and F. P. Fischer discuss in German The Mechanics of the Tissues Composing the Eye. There is a summary in French. Gosta Karpe of Stockholm writes in English on an Apparatus and Method for Clinical Recording of the Electroretinogram and on the Early Diagnosis of Siderosis Retinae by the use of Electroretinography. Finally, L. Poleff of Rabat writes in French on Experimental Pathology of Trachoma.

E. J. S.

BOOKS RECEIVED

1. Report of the Committee on Indigenous Systems of Medicine. Volume I:—Report and Recommendations. Published by the Ministry of Health, Government of India. 1948. Pp. 200.

2. Report of the Committee on Indigenous Systems of Medicine. Volume II:—Appendices. Published by the Ministry of Health, Government of India. 1948. Pp. 550.

3. Proceedings of the National Institute of Sciences of India. January 1949. No. 1, Volume XV, Pp. 1-24. Published by the National Institute of Sciences of India, Delhi.

Abstracts from Reports

ANNUAL PUBLIC HEALTH AND VACCINATION REPORT OF THE PROVINCE OF ORISSA FOR THE YEAR 1944. PUBLISHED BY THE SUPER-INTENDENT, ORISSA GOVERNMENT PRESS, CUTTACK. Pp. 79. PRICE, Rs. 3-5-6 or 5s.

Births.—The total number of live births recorded in 1944 was 195,835 against 237,023 in 1943 showing a decrease of 41,188 births in 1944. The birth rate was 25.25 against 30.75 in 1943. This is a feature generally observed during war when men undertake service far from home; but has probably been contributed to chiefly by the conditions of under nourishment and distress resulting from the increased cost of foodstuffs.

Deaths.—The total number of deaths registered in 1944 was 235,581 against 233,584 in 1943. The death rate was 30.36 in 1944 against 30.30 in 1943.

Infantile mortality.—There were 40,784 infantile deaths registered in 1944 giving an infant mortality rate of 208.26 per 1,000 live births as compared with 202.55 in 1943.

Of the total number of deaths recorded 40,784 or 17.31 were under one year against 20.55 in 1943.

The high mortality rate among women in the reproductive period and the high infant mortality figure indicate, as reported in the previous years' reports, that steps should be taken to make adequate provision for maternity and child welfare services in the Province.

Cholera.—The total number of deaths recorded from cholera in 1944 was 18,246 against 20,502 in 1943.

In an endemic coastal area of Cuttack district mass inoculation was carried out as an experimental measure and it was found that although cholera in epidemic form broke out around, this area was totally free from the disease.

Smallpox.—The total number of deaths from smallpox in 1944 was 8,124 against 4,244 in 1943.

852,780 doses of vaccine lymph were purchased by Government of Bihar at Namkum and were supplied free of cost for vaccination in the Province.

Dysentery and diarrhoea.—There were 18,803 deaths from this group of diseases against 19,165 in 1943.

Respiratory diseases.—4,613 deaths were recorded from respiratory diseases in the Province in 1944 against 4,821 deaths in 1943.

Deaths from pneumonia and pulmonary tuberculosis which are included among those from respiratory diseases probably claim quite a big percentage of total deaths recorded under this cause.

There is only one tuberculosis clinic in the Province situated in the premises of the Cuttack General Hospital.

During the year under report 428 patients, including 37 carried over from the previous year, attended the clinic.

Fairs and festivals.—At the time of the *Car Festival* at Puri the health condition of the neighbouring provinces, viz, Bihar, Bengal and Assam, from where a large number of pilgrims usually come to Puri to witness the festival, was very unsatisfactory. In fact about 3,000 attacks from cholera per week were reported from certain parts of Bihar. So it was necessary to make elaborate sanitary and preventive arrangements during the festival period from the 5th June to the 4th July, 1944, to prevent a serious epidemic of cholera at Puri which might possibly spread far and wide in the Province.

Local arrangements.—Arrangements to isolate all cases of cholera for proper treatment were made in

the Puri Government Headquarters Hospital. There was no epidemic of cholera in the festival area before the *Car Festival*. With the arrival of pilgrims in very large numbers immediately before the *Car Festival* a mild epidemic of cholera broke out. There were 64 attacks and 17 deaths. The epidemic was brought under control within a short period.

Fevers.—In 1944 fevers alone accounted for 129,273 deaths. This constitutes 54.87 of the total mortality.

Malaria.—The malaria problem of Orissa is extremely varied and complex.

Anti-larval operations were carried out at Government cost at Koraput, Jeypore, Malkangiri, Pottangi, Bissamecuttack and Nandapur in the district of Koraput.

In all these centres paris greening of breeding places of mosquitoes, canalization of stagnant waters and weed clearing were done. Systematic spraying of pyrethrum extract was not practised as no pyrethrum is being released for civil use which is very disappointing. The need for the extract is keenly felt among the civil population which merits serious consideration.

Anti-mosquito schemes were also carried out with Government aid in the Municipalities of Cuttack, Puri, Balasore, Kendrapara, Berhampur and Sambalpur. Anti-mosquito measures were handicapped by lack of pyrethrum extract.

At Balugaon in the district of Puri malaria broke out in epidemic form during the summer months and several deaths were recorded. As a measure of control, free distribution of quinine and quinine substitutes was done in the affected areas by appointing one temporary epidemic doctor and two temporary health inspectors.

In Ganjam plains there was widespread epidemic of malaria in Chatrapur, Berhampur (South), Berhampur (North) and Kodala ranges during the year. For the group of villages round about Hinjili in the Chatrapur range an emergency hospital was opened for about 2½ months, in addition to other anti-malaria measures, viz, distribution of quinine, clearance of weeds, etc. The situation was also complicated for want of food and consequent nutritional disorders. The epidemic was however brought under control in a short time.

Maternity and child welfare work.—During the year under review the Maternity and Child Welfare Centres at Cuttack, Berhampur and Sambalpur continued to function each under the supervision of a qualified health visitor. Eleven more centres carried on their activities.

School hygiene and medical examination of school children.—Nutritional deficiency amongst the students has been a problem in this Province. During the year under report 19 per cent of students were found with distinct signs of malnutrition and 8.7 per cent with marked signs of avitaminosis. Provision was made in many schools to supply some nourishing tiffin, milk and calcium lactate to the students; but due to high price of the food-materials, the practice has been given up in most of the schools. Some of the schools however distributed dried milk and multivitamin tablets supplied by this Department.

5.1 per cent of the students were found to be unprotected against smallpox.

Vaccination.—The total number of primary vaccinations performed in 1944 was 233,276 as compared to 238,609 in 1943 showing a decrease of 5,333 in 1944.

848,734 persons were revaccinated in 1944 as against 805,712 in 1943 showing an increase of 43,022.

As no arrangement exists in this Province for the manufacture of vaccine lymph, the requirement of vaccine lymph is purchased from the vaccine institute of the Government of Bihar at Namkum and supplied free of charge in the Province. 852,780 doses of vaccine lymph were purchased by Government at a cost of Rs. 22,207-13-0 during 1944.

The provisional, pathological and public health laboratory.—The total number of samples examined in

the laboratory was 13,137 in 1944 against 8,488 in 1943. Of these 224 were samples of water, 328 were samples of food-stuffs and 12,585 were pathological specimens including specimens of blood tested in connection with blood transfusion service.

Work on the pathological side is increasing year after year. In all, 12,585 specimens were examined against 7,912 in 1943 and 5,464 in 1942. Samples were received from all over the Province.

Conclusion

This was another testing year which the Department had to pass in a tense atmosphere that has been prevailing in the country since the outbreak of war. Food shortage and economic depression together with the heavy influx of people enhanced the gravity of the health problems already in existence or created by natural and social conditions peculiar to the Province. While the neighbouring provinces of Bihar, Bengal and some parts of Madras suffered from heavy catastrophes the Province could fortunately be prevented from sharing the same lot.

Correspondence

MICROFILM SERVICE UNITS

SIR,—Your publication from the Circular No. F.S/OSR (2R)/48-908, dated 14th October, 1948, from the Department of Scientific Research, Government of India, New Delhi, concerning Microfilm Service Units set up by the Indian Research Fund Association at the Central Research Institute, Kasauli, and at the Tata Memorial Hospital, Bombay, has been passed to us by one of our customers. We note that you refer your clients to us in order that they may obtain a Microfilm Reader.

For this we indeed thank you but would like to point out that the Reader in question, called the Spencer Microfilm Reader, is manufactured in the U.S.A. and at the moment we are unable to obtain supplies as we do not hold the necessary import licence. Prospective customers have therefore to obtain their own licence, when we are only too pleased to place an order for them with the Eastman Kodak Co., Rochester, U.S.A. The current price is, as stated by you, Rs. 300.

Yours faithfully,
KODAK LIMITED,
P. H. HEILBRON.

TUBERCULOSIS

SIR,—Concluding the review of the Australian scheme against tuberculosis in the *Indian Medical Gazette* of September 1948, you remarked that 'those who advocate a similar scheme for India would do well to remember that "tuberculosis is a dying disease".'

Since 1934 onwards almost every year the Public Health Commissioner's reports have been warning that the disease is on the increase in India (and in urbanized industrial areas particularly). Recent reports show that about 60,000 deaths a year are being officially reported and suggest that 20 per cent of all the deaths attributed to respiratory diseases and 10 per cent of all those attributed to 'fevers' should be counted as tuberculosis mortality. On these suggestions Bhole Committee estimated an annual death rate of about 450 thousand to 800 thousand, i.e. 165 per 100,000 of population and about 7 per cent of all deaths. This is surely worse than any country where active measures are in practice for some time. No one

in those countries seriously thinks that the disease is dying although the mortality is dropping considerably.

It has been shown repeatedly that the incidence of tuberculosis fluctuates with the socio-economic fluctuations in a community, and that these fluctuations are very sensitive. During the hard period of 1912-43 the death rate, which was hitherto well under control, suddenly jumped up and the peak-age of death shifted down to 25-30 years of age; this demonstrates the sensitivity. Our social and economic conditions are, surely, not very stable.

Vast majority of our population is not yet exposed and will fall an easy prey once the disease enters (and industrialization and urbanization will introduce it) these untouched areas. Our present measures are not sufficient even for our present essential needs let alone these emergencies if such arise.

We do not see why we in India should say that it is a dying disease.

Yours faithfully,
M. S. KATARIA.
S. Y. BHAGWAT.

46, KENSINGTON GARDENS SQUARE,
LONDON, W.2.

15th February, 1949.

[The subject is fully discussed in the editorial entitled 'Incongruities in tuberculosis and associated considerations', *I.M.G.*, January 1948, page 41.—Editor, *I.M.G.*]

B.C.G. VACCINE

SIR,—I shall feel thankful if you would be good enough to supply me with detailed information about a disaster that occurred in a village in Germany, several years ago, which followed inoculation of children with B.C.G. vaccine and in which several deaths had occurred in the inoculated children due to some mistake or misadventure on the part of the doctors and a noted pathologist was sentenced to imprisonment as a result of inquiry set up to find out the causes of the disaster.

Yours faithfully,
K. V. THAKKAR, L.M.S.,
President, City Municipality.

BHAVNAGAR,
31st January, 1949.

[This tragedy occurred at Lubeck in Germany during the winter of 1930-1931. The judicial trial which began on 13th October came to an end on 6th February, 1932.

Prof. Deycke and Dr. Altstadt were both found guilty of manslaughter by negligence in 68 cases and of causing injury by negligence in 131 cases. They were sentenced to 2 years and 1½ years' imprisonment respectively. Prof. Klotz and Nurn Schutz were found not guilty and acquitted, the charges against them not being sufficiently proved.

It was held that the disaster was caused by an exchange of B.C.G. with other virulent bacilli or by contamination. Prof. Deycke had prepared the culture in a laboratory where contamination of exchange was possible. Dr. Altstadt had not got the culture tested before distribution and had not stopped the distribution immediately after being informed by Prof. Deycke that something was wrong with them.

253 infants in Lubeck had been given by the mouth B.C.G. vaccine sub-cultured from cultures received from the Pasteur Institute of Paris. Within some 3 months 68 had died of acute tuberculosis and doubt had arisen on the nature of the vaccine. Had B.C.G. suddenly become virulent or had some other strain of tubercle bacillus gained access to the vaccine

accidentally? The court had decided for the latter occurrence.

Further details will be found in the *Lancet*, 13th February, 1932, pp. 353 and 365.

Extensive experience of bacteriological laboratories all over the world has shown that there is little inclination for the B.C.G. culture now in use to increase in virulence, whatever may have been the virulence of the strain in the earlier days of the experiment. Even deliberate attempts in the laboratory to enhance its virulence have repeatedly failed. These observations lend support to Calmette's claim that B.C.G. is a *virus fixæ*. Indeed, some, reputed B.C.G. experts, notably Prof. Wallgren of Stockholm, believe that 'it is, however, not inconceivable that B.C.G. finally may become so avirulent as to have no effect.'—EDITOR, *I.M.G.*

CORNEAL GRAFTING IN INDIA

SIR,—I request you to kindly inform me if there is any ophthalmic surgeon in India who performs keratoplasty (transplantation of cornea).

Yours faithfully,
IKRAM-UD-DIN ABBASI.

HAFIZABAD,
17th March, 1949.

[Reference may be made in this connection to the article entitled 'Corneal grafting in India: Its difficulties', published in the *I.M.G.*, November 1947, p. 676.—EDITOR, *I.M.G.*]

Service Notes

LEAVE

Lieutenant-Colonel W. T. Taylor, lately Additional Deputy Director-General of Health Services (Stores), was granted war leave on average pay for 28 days combined with extraordinary leave for 3 days with effect from the 26th August, 1946.

Lieutenant-Colonel M. L. Ahuja, Director, Central Research Institute, Kasauli, was granted leave on average pay for 15 days with effect from the 25th January, 1949.

RELINQUISHMENTS

The undermentioned officer relinquished his E.C. in I.M.S. and was also released from I.M.D. now I.A.M.C. (S.M.S.) w.e.f. the date specified against his name, on being granted short service commission in the R.A.M.C.:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Major D. H. Niblett. Dated 11th June, 1947.

The undermentioned officer is permitted to relinquish his commission on release from the army service, with effect from the date shown against his name and is granted the honorary rank of Lieutenant-Colonel:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
(Emergency Commission)

Major Bhupes Chandra Roy. Dated 30th December, 1945.

The undermentioned officers are permitted to relinquish their commissions:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captain T. E. Unny. Dated 18th March, 1946.

Captain S. K. Puri. Dated 26th April, 1946.

Captain S. C. Ghosh. Dated 10th May, 1946.

Captain A. B. Talibbudin. Dated 29th May, 1946.

Major R. Kasliwal. Dated 5th June, 1946.

Captain M. L. Bhagata. Dated 4th June, 1946.

The undermentioned A.I.R.O. (M.) officers relegated to reserve on release from mobilized service, on the dates shown against their names, are granted honorary rank, as shown in brackets:—

ARMY IN INDIA RESERVE OFFICERS (MEDICAL)

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

Major L. R. Kapoor (Major). Dated 13th February, 1947.

Major C. S. Ahluwalia (Captain). Dated 5th November, 1947.

Captain B. Das (Major). Dated 5th January, 1947.

Major S. J. Sane (Captain). Dated 19th August, 1947.

Captain D. N. Chakravarty (Captain). Dated 17th January, 1947.

Captain S. C. Banerjee (Captain). Dated 26th October, 1946.

Major P. V. Gharpure (Major). Dated 17th April, 1947.

Captain G. Singh (Captain). Dated 28th January, 1947.

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Communications for the Publishers relating to Subscriptions and Advertisements should be addressed to THE PUBLISHERS, *The Indian Medical Gazette*, P. O. Box No. 54, Calcutta.

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Original Articles

STREPTOMYCIN THERAPY IN TUBERCULOSIS

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THE following is a report on the effect of streptomycin in twenty-one suitable cases of tuberculosis treated in the Hardinge Hospital (Dharampore and Arcadia Dharampore) during the year 1948.

Clinical material.—All patients in this series had pulmonary tuberculosis which, prior to streptomycin therapy, had not responded to bed-rest or other accepted forms of treatment. There was roentgenographic evidence of recent progression in their pulmonary lesions and the sputum was positive in all.

Age and sex.—Thirteen patients were male and eight female. One patient was five years old, one was forty-seven years old, and the rest were between the ages of 15 and 35 years.

Extent of the disease.—This is tabulated below.

TABLE I

Distribution of patients according to the extent of the disease

Extent of the disease	COMPLICATIONS		
	Intestinal involvement	Laryngeal involvement	Diabetes
Unilateral lesion without cavitation	1	0	0
Unilateral lesion with cavitation ..	3	0	0
Bilateral lesion without cavitation	2	0	1
Bilateral lesion with cavitation in one lung ..	13	3	0
Bilateral lesion with cavitation in both lungs ..	2	2	0
TOTAL ..	21	5	1

Four patients had unilateral lesions, in which artificial pneumothorax treatment had not been successful, and seventeen had bilateral lesions. Five of the latter had intestinal tuberculosis, one had laryngeal tuberculosis, and one had diabetes in addition to the pulmonary disease. Eighteen patients had definite cavities as seen in radiological examination. In six patients the cavities were multiple and large, and in the rest there were small ones. Three bilateral cases had artificial pneumothorax on the side of the

extensive lesion, and the same was maintained during the streptomycin treatment.

Dose and method of administration.—One gramme of streptomycin was given daily in two divided doses morning and evening for a period of ninety days in all these cases except two in which the treatment had to be stopped after thirteen and twenty-one days respectively. No attention was paid to individual differences in body-weight, all patients receiving the same amount of drug.

The solution was prepared by adding 6 cc. of distilled water and 2 cc. of 1 per cent procain solution to the 1 gramme of streptomycin in its original commercial container. Half of this solution was injected intramuscularly in the morning and the other half in the evening. This dose was tolerated well.

One patient, who was suffering from laryngeal tuberculosis, was given streptomycin spray in addition to the injections. There being no proper instrument for aerosol therapy, an ordinary throat spray was used for this purpose. One gramme of streptomycin was dissolved in 8 cc. of water, and this was slowly sprayed in the throat by the patient himself, while he kept on breathing normally. The solution was sprayed every two or three hours, and the whole of eight cubic centimetre solution was sprayed in twenty-four hours.

In two patients a second course of streptomycin for thirty days and forty-five days respectively was given two months after the completion of the first course of ninety days, as these patients showed relapse of clinical symptoms, and progression of the disease. The condition of both these patients was controlled by this further medication with streptomycin.

TABLE II
Toxic reactions

Severity	Vestibular disturbances	Skin rash	Loss of appetite	Nausea	Sensation of heat in the head
Slight ..	17	3	5	8	2
Moderate ..	3	2	0	1	0
Severe ..	1	0	2	0	2
TOTAL ..	21	5	7	9	4

(1) *Local reaction.*—Pain at the site of intramuscular injection was scarcely greater than that encountered with any other injection. One lot of streptomycin gave more severe local reactions and its use had to be given up on this account. The injections were given in rotation in the arms

and the buttocks. No skin infection or subcutaneous abscess developed in any case.

(2) *Vestibular disturbances.*—These disturbances occurred in all these cases, but were not severe in the vast majority of these patients. They were manifested most frequently by a dizzy or a light-headed sensation noted on sitting up in bed. The walking patients experienced difficulty in properly maintaining their balance while out of bed. The vestibular disturbances occurred from tenth to seventeenth day and persisted throughout the treatment, and to some extent, in some cases long after stopping the treatment. Slight deafness occurred in one patient who was forty-seven years old.

(3) *Skin rash.*—An urticarial rash occurred in five patients. The rash occurred after twelve days in three, and after seventeen days in two patients. The rash however faded promptly on benadryl administration.

(4) *Loss of appetite.*—Severe loss of appetite was felt by two patients, whose disease was in an advanced stage and who later died. Slight loss of appetite was felt by two other patients, and in these the treatment had to be interrupted for a few days on this account. The rest of the patients showed a marked increase in their appetite.

(5) *Sensation of heat in the head.*—Some patients felt a queer sensation of heat in their head, and in two of them it was so severe that this treatment had to be stopped. These were the same patients who had experienced severe loss of appetite.

(6) *Nausea.*—Slight nausea occurred in about half the patients, but it did not give much trouble, and disappeared by itself on continuing the treatment.

Renal damage.—There was no evidence of renal irritation in any of these cases. One patient, who had bilateral exudative pulmonary lesion, was also found to be passing albumin in his urine. Quantitative analysis showed it to be about 0.175 per cent. He was put on streptomycin treatment. His urine was examined on every alternate day, and it did not show any increase in albumin, or showed the presence of any cast during the treatment. He showed marked improvement clinically as well as radiologically (see skiagrams, nos. 1 and 2).

TABLE III

Clinical observations during therapy

	Number	Extent
Weight increase ..	19	12 pounds
Appetite increase ..	19	Marked
Cough decrease ..	18	Do.
Sputum decrease ..	18	Do.
Temperature decrease ..	19	Do.
Sedimentation decrease ..	16	Do.

Marked improvement was seen in the clinical symptoms in a very large number of these cases. Temperature came down in nineteen patients within the first three weeks. Increased appetite was noted in all but two. Cough and expectoration decreased in the majority within two weeks. Weakness and fatigue decreased in most of them after the first month of the treatment. The pain in the abdomen and other intestinal symptoms showed a marked relief in all the five cases who showed these symptoms. One patient who had laryngeal trouble also showed great improvement.

Three patients in whom the indication of major surgery, which could not be considered before, because of the advanced state of the disease, and precarious general condition, which was far below the minimal requirement for surgical intervention, became suitable for thoracoplasty after streptomycin therapy.

There was a constant but gradual lowering of the temperature. The more toxæmic patients showed the greater decrease in temperature. The temperature came down to normal and remained so in seventeen cases. In one advanced case the temperature came down to subnormal, and the patient later died. The pulse rate did not decrease in proportion to the temperature.

Cough decreased to a marked degree in eighteen patients within the first three weeks. In one patient the cough did not show any decrease. As his sputum showed pneumococci in abundance, he was put on penicillin treatment for six days, and his cough subsided markedly on this treatment. Streptomycin administration was carried on after this treatment as before.

The average volume of sputum decreased, and after first month of treatment most of the patients were not bringing out more than one-third of their previous volume. Four patients did not bring up any sputum at all. The sputum also became thinner and less purulent.

There was gain of weight in nineteen out of the twenty-one cases and it ranged up to twenty-seven pounds, with an average gain of twelve pounds per patient. The maximum gain of weight occurred during the first month of the treatment. Only one patient who was very advanced showed loss in weight and died during the course of treatment.

Two patients in this series had been put on streptomycin as they had developed widespread disease in both the lungs after a profuse and prolonged attack of hæmoptysis. Both these patients showed great improvement clinically as well as radiologically. One case, however, got a fresh attack of hæmoptysis one month after the treatment with streptomycin had stopped. The frequency and severity of hæmoptysis remained unaltered during the treatment of two other cases, who were having attacks of hæmoptysis off and on during the treatment.

Diabetes.—One case of pulmonary tuberculosis had also diabetes. In the treatment of this case streptomycin treatment was associated with the use of insulin in adequate doses, and the patient showed marked improvement clinically, but the improvement was not so marked radiologically.

Laboratory observations: (1) *Sputum.*—Sputum of every patient was examined for the presence of tubercle bacilli at the start of the streptomycin treatment, and was examined every two weeks till the treatment was completed. Sputum was examined by ordinary smear method only. All the patients in this series showed tubercle bacilli in their sputum at the beginning of the treatment, while only fifteen showed the presence of tubercle bacilli at the end of the treatment. The sputum of these six negative cases was further examined three times in a week for two weeks, and it confirmed the earlier findings.

(2) *The erythrocyte sedimentation rate (Westergren's method).*—This was taken once at the start of the treatment, then fortnightly till the treatment was completed. A definite reduction of rate occurred during therapy in a number of cases, though the extent of reduction, like that of the original increase, was variable. It showed a decrease of more than fifteen millimetres per hour in eighteen cases, remained practically the same in two cases and showed an increase after initial decrease in one case.

(3) *Urine.*—Urine analysis of every patient was done at the start of the treatment, it was done thrice in a week during the first month, and twice in a week during the second and third month. No renal irritation, as evinced by the presence of albumin, or cast in the urine was shown in any of these cases. One patient, who was found to be passing albumin in his urine at the start of the treatment, continued to do so during the treatment, without showing any increase in the quantity of albumin, or any cast in it.

Roentgenographic observations.—Every patient had a skiagram taken at the start of the treatment, and after that it was taken every month till the completion of the treatment. Radiological improvements were seen, but these were not as quick as the clinical improvements for obvious reasons, and were variable depending on the type and extent of the lesions.

The most marked resolution noted in the chest roentgenograms occurred in soft, nodular, and exudative type of infiltrations. Two patients showed nearly a complete disappearance of exudative component of their disease, one (case 2) had extensive disseminated soft shadow lesions, and the other case (case 4) had moderately advanced pulmonary tuberculosis with a small cavity. Eight patients were deemed to have marked resolution, six moderate, and three slight resolutions, two remained unchanged. Infiltrations of fairly recent occurrence showed

moderately good response to therapy, whereas similar lesions of long standing showed very little response.

Lobar or segmental consolidation was present in six cases, in none did complete resolution occur. There was marked clearing in one, and moderately appreciable clearing in the rest.

Cavities were present in eighteen patients. Out of these two had cavities in both lungs, two had giant cavities, twelve had cavities of moderate size, while five had only small cavities.

In patients who had large cavities, the size remained practically the same, though the general health of the patients improved to such an extent that in three of them surgery could be performed. The cavities were deemed to have closed in three cases, decreased moderately in four cases, slightly in seven cases, and they remained unchanged in the rest. Decrease in the zone of reaction in the parenchyma surrounding the cavities was a fairly consistent finding. Ten patients, who showed fluid level in their cavities before the treatment, did not show any fluid level at the end of the treatment.

Case reports

Case 1.—S. L., no history of tuberculosis in the family.

The patient had weak health since he was born and had specially weak digestion. He could not even walk properly at the age of 5 years.

The patient suddenly got ill with fever and bronchitis on 6th May, 1948, and was treated as a case of typhoid fever at Ambala. X-ray skiagram was taken on 24th June, 1948, and showed widespread non-confluent lesions in both the lungs (figure 1, plate XII). The whole of the right lung was studded with soft non-confluent spotted opacities, not miliary but discrete. Left lung also studded with the same sort of spotted opacities but less in number and extent. Sputum was examined on 27th June, and was found to contain tubercle bacilli.

The patient was brought to me on the 29th June, 1948, in a very weak condition. He was much emaciated. His temperature was 102.4°F., cough was persistent. He had diarrhoea and his abdomen was tender on palpation. I had not much hope about the case, but considering the widespread non-confluent exudative lesions and the involvement of intestine, I put him on streptomycin on 2nd July, 1948. The patient showed a very marked improvement as is clear from the study of the x-ray skiagram. He got a great relief in the clinical symptoms (figure 2, plate XII). In the right lung, a great part of the spotted opacities cleared and in the left lung only calcified spots seen in the hilar region, otherwise the lung field practically clear. Some soft mottling was seen in both the lungs especially in the right mid-zone.

Case 2.—R. D. Family history: Younger sister died of tuberculosis 2 years back.

The patient had a fairly good health and did not suffer from any particular disease excepting an attack of cold off and on.

The patient got ill with fever on 7th March, 1948. There was also slight cough. As there was history of tuberculosis in the family, the patient got himself x-rayed on 12th March, 1948. The x-ray showed extensive bilateral exudative lesion (figure 3, plate XII): In the right lung, supraclavicular region is dull and showed patchy opacities, rest of upper and middle zones showed multiple lesions of cotton-wool appearance, shades of white and grey overlapping each other with cavity formation, lower part of the lower zone being free. In the left lung, upper and middle zones showed exudative process with signs of destruction in centre, lower zone shows marked lung structure. The sputum was examined on 16th March, 1948, and was found to contain tubercle bacilli.

The patient came under my treatment on 16th May, 1948. A.P. was tried on right side but failed. In view of the extensive exudative lesion, streptomycin was started on 24th May, 1948, and was continued for 3 months.

The patient showed a marked improvement clinically as well as radiologically (figure 4, plate XII). In the right lung, upper and middle zones showed partial disappearance of the exudative process and its replacement with fibrous tissue, and cavity smaller than before. In the left lung, the exudative process in the upper and middle zones showed partial resolution and replacement by fibrous tissue, and linear strands and stripes are present.

One important thing in this case was that the urine of the patient was found to contain traces of albumin before the streptomycin treatment was started. I could not decide whether I should start giving injections of streptomycin in the presence of albumin in the urine. As the case was quite extensive, I took the chance and started giving streptomycin. The urine was examined daily for the most part of the treatment and the quantity of albumin did not increase at any time.

Case 3.—H. D. Family history: His brother's wife died of tuberculosis 2 years back.

The patient had a weak constitution and suffered from a number of diseases—measles, pneumonia and typhoid fever—in his childhood.

The patient suffered from slight fever and cough in the month of January 1948, and was treated at his own home by local hakims. As the fever did not subside, his x-ray was taken on 1st April, 1948, and was found to be suffering from pulmonary tuberculosis of the right lung. His sputum was examined and was found to contain tubercle bacilli. He joined King Edward Sanatorium, Dharampore, in May 1948, where A.P. was tried but failed. His condition did not improve and his x-ray

skigram taken on 26th June, 1948 (figure 5, plate XIII), showed further extension of the disease: whole of upper and middle fields opaque with patchy dullness and multiple areas of destruction, lower zone cotton-wool appearance, shadows right lung, and it spread also to the left lung, presence of soft shadows (exudative process) in all three zones.

He came under my treatment on 29th June, 1948, and I put him on streptomycin on 3rd July, 1948.

The treatment is in progress and the patient has shown a very marked relief in his clinical symptoms. Improvement is also shown radiologically (figure 6, plate XIII): right lung, density of shadows in upper and middle zones much less showing partial resolution of the exudative process and its partial repair by fibrous tissue, cavities still present; left lung, density of shadows in upper and middle zones much less and lung structure more marked in lower zone. During earlier part of the treatment, the patient suffered from night sweats which were very profuse. These also disappeared after 20 days of treatment.

Case 4.—B. K., before treatment, extensive bilateral exudative pulmonary lesions with cavitation in the right lung (figure 7, plate XIII).

After treatment, the exudative lesion in the left lung has cleared to a great extent; the right lung shows satisfactory collapse. The cavity appears to be collapsed. A number of thick pleural adhesions are seen (figure 8, plate XIII).

Summary

1. An account of twenty-one pulmonary tuberculosis cases treated with streptomycin during the year 1948 is given.

2. One gramme of streptomycin was given in two divided doses. This dose appears to have been tolerated well. The writer believes that good results can be obtained with this dosage, which is not only economical, but also prevents toxic reactions of an irreversible type.

3. Symptomatic improvement as evinced by decline of temperature, lessening of cough, improvement of appetite and increase in weight was seen in more than 80 per cent of these cases, and were more marked during the first month of the treatment.

4. The drug did not seem to have any beneficial influence on the occurrence of hæmoptysis. Patients who were having attacks of hæmoptysis before the treatment continued to have them during the treatment as before.

5. Radiological improvement did not go hand in hand with clinical improvement. The most marked resolution occurred in soft, nodular, and exudative type of infiltration of recent origin. Consolidations and confluent infiltrations did not show the same response. Fibro-calcious lesions did not show any regression.

6. Small cavities did close with this treatment, but cavities of large size were not affected. Their

walls however appeared thinner, and most of them did not show any fluid level as they did before the treatment.

7. The toxic reactions to streptomycin with one gramme dose were quite mild, and of reversible type.

8. From the above the writer concludes that streptomycin has a marked beneficial effect in pulmonary tuberculosis. It may however be added that streptomycin is not the complete treatment of tuberculosis, nor is it useful in all types of cases. It is only a part of a treatment, at a certain stage, and must be regarded as ancillary to bedrest, sanatorium regime, and in some cases collapse therapy, and not a substitute for them.

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[Further progress of these cases, including observations on drug fastness of the mycobacterium, will add valuable information to our knowledge of streptomycin therapy in pulmonary tuberculosis.—EDITOR, *I.M.G.J.*]

GUMMA OF THE HEART

A REPORT OF THREE CASES

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SYPHILIS of the heart can be divided into two distinct groups. In the first, there is diffuse inflammatory reaction with interstitial connective tissue proliferation and fibrosis; this was described by Warthin (1925) as syphilitic myocarditis. He claimed to have demonstrated *Treponema pallidum* in such lesions. However, many others working on the same subject have not succeeded in demonstrating the organism. There is, therefore, a marked difference of opinion as regards the syphilitic basis for this lesion. The other lesion is of the gummatous variety and this may take either a localized or a diffuse form. This type of lesion is met with in congenital as well as in acquired syphilis.

Amongst the tertiary syphilitic lesions, gumma of the heart has always been a rare lesion and with the proper treatment of syphilis it is likely to be rarer still in future. Ricord (1845) described the first case of gumma of the heart. Sohval (1935) wrote that up to date only 97 authentic cases of gumma of the heart had been reported and added two more cases. A review of the literature up to date showed 109 authentic

cases of gumma of the heart. The present writer describes the following three cases.

Case reports

Case 1

Clinical notes.—A male, aged 40 years, was admitted into the hospital for pain in the abdomen and vomiting. The duration of this complaint was two days only. The pain started in the epigastrium, was dull in character and had no relation to food. He had vomited four times. The pain had gradually increased and had become generalized all over the abdomen. There was no history of a similar attack in the past. There was tenderness and rigidity of the upper abdomen, and the peristaltic sounds were not heard. Examination per rectum also elicited tenderness. His general condition was low. His blood pressure was 90/60. Examination of the urine did not reveal any abnormal constituent. Exploratory laparotomy was performed but nothing abnormal was detected in the abdominal cavity. The abdomen was closed. The patient expired 3½ hours after admission.

Autopsy notes.—The heart (figure 1, plate XIV) weighed 400 gm. and was enlarged, especially its left side and its right side was engorged. Minute epicardial hæmorrhages were present near its apex and in the right atrium. The apical region showed an abrupt change in its consistency, being soft to feel. On opening the heart, the right atrial wall was thinned out due to dilatation of the chambers. The right ventricle did not show any abnormality. The left atrium was normal. The endocardial surface of the left ventricle near its apex was rough and covered with ante-mortem thrombi. The interventricular septum showed a large white area about 5 cm. by 6 mm. extending from the membranous portion above to its attachment below. This area had involved the anterior wall of the left ventricle and had extended towards the endocardial surface to produce a white thickened patch of fibrosis. Surrounding this area there was a zone of hyperæmia. Such an extensive lesion had probably involved the bundle of His. The coronary openings were slightly dilated and the coronary arteries showed a few atheromatous patches along their course. Both of them were dissected but no thrombus could be detected. The pulmonary artery and the aorta showed early atheromatous change. The naked eye diagnosis was massive cardiac infarction. Sections (figure 2, plate XIV) stained with H&E. stain showed the following features: An extensive area of necrotic granular debris, in which ghosts of myocardial fibres undergoing hyaline change and necrosis were seen. This area was fairly well demarcated from the rest of the tissue by a zone of newly formed capillaries and proliferating fibroblasts. In this zone the cellular reaction consisted of a large number of lymphocytes, a fair number of plasma cells, and an occasional

eosinophil and macrophage. Giant cells were not seen. The cells were distributed perivascularly and the endarteritic process could be seen in some of the blood vessels. Myocardial fibres round about the lesion showed various degrees of degenerative changes. The sub-endothelial connective tissue showed proliferative changes and was infiltrated with mononuclear cells. Ante-mortem thrombi could be seen on the endocardial surface. There was an increase in the connective tissue round the branches of the coronary arteries (figure 3, plate XIV) and some of them showed endarteritic changes. Myocardial fibres, far beyond, did not show any hypertrophic change. Sections stained by Ziehl-Neelsen's method did not reveal the presence of mycobacterium tuberculosis. Sections could not be stained by Levaditi's method as the tissue was fixed in 10 per cent formalin saline. The lungs showed fibro-caseous tuberculosis and the liver showed changes of chronic passive congestion.

Case 2

Clinical notes.—A female, aged 30 years, was admitted for weakness, loss of appetite, duration three months, and oedema of the feet. There was puffiness of the face and the neck veins were prominent. There was free fluid in the abdomen and the liver was enlarged and tender. Her B.P. was 110/65. She expired within 4 hours of admission.

Autopsy notes.—There was generalized anasarca and marked pallor of the mucous membranes. The heart (figure 4, plate XIV) was twice the normal size, soft to feel and its right side was engorged. The left ventricle was soft and flabby. On the anterior surface of the heart were several petechial hæmorrhages. On opening the heart, the myocardium was found to be thickened and in the wall there were multiple whitish nodules firm in consistency, varying in size from 2 mm. to 1 cm. in diameter. The walls of both the ventricles were involved, the left being more extensively affected. At the apex of the heart the left ventricular wall was thinned out and there was an early aneurysmal dilatation about 2 cm. in diameter. It was covered with an ante-mortem thrombus. Sections (figure 5, plate XIV) stained with G.&E. stain showed multiple gummata. There were several areas of necrosis surrounded by newly formed capillaries and proliferating fibroblasts. The granulation tissue was densely infiltrated with plasma cells and lymphocytes. Several giant cells could be seen amongst the inflammatory cells. Changes of endarteritis and periarteritis were also seen. The aorta and the coronary arteries were normal. The liver showed changes of chronic passive congestion.

Case 3

Clinical notes.—A female, aged 40 years, was admitted in an unconscious state. On admission,

her temperature was 97°F., and the pulse was feeble and rapid. The liver was palpable just below the costal margin. She expired within half an hour of admission.

Autopsy notes.—The pericardium was adherent to the sac of the aneurysm. The pericardial fluid was clear, yellow in colour and increased in amount. The heart weighed 665 gm.; it was enlarged, pale, flabby to feel and the epicardial fat was diminished. The apex was enlarged into an aneurysmal sac involving the left ventricle. The wall of the sac was very thin and was on its inside covered with ante-mortem thrombi. Sections (figure 6, plate XIV) from the left ventricular wall showed histologically the structure of a typical gumma. Amongst the inflammatory cells an occasional giant cell could be seen. The aorta showed atheroma but no evidence either naked eye or microscopically of syphilitic infection. The liver and the spleen showed changes of chronic passive congestion. The left kidney showed the presence of a calculus and changes of hydronephrosis.

COMMENTS

In the myocardium a localized gumma is more common and typical in its histological structure than a gumma elsewhere in the body. There may be a single gumma or a conglomeration of multiple minute gummata, the latter being more common. Diffuse gummatous myocarditis with unrecognizable gross gummata is a very rare condition. The size of the multiple gummata varies from 2 mm. to about 3 mm. in diameter. They are dull yellowish or greyish white in colour and rubber-like in consistency. These can occur anywhere in the heart but the commonest is the left ventricular wall especially at the base of the interventricular septum, often giving rise to symptoms and signs of heart-block. The endocardium and the epicardium overlying the lesion show sclerotic thickening. In rare instances partial obliteration of the pericardial cavity may be produced. A gumma may heal by fibrosis and occasionally with calcification, or may undergo extensive softening which may lead to a cardiac aneurysm.

For definite histological diagnosis of gummatous myocarditis Sohval (1935) has established the following criteria: (1) Widespread perivascular and interstitial granulation tissue infiltrated with lymphocytes and plasma cells. (2) Process of endarteritis going on to obliteration. (3) Areas of coagulative necrosis. (4) The presence of myocardial fibres in the necrotic area helps to differentiate a gumma from a tuberculoma. He attaches great importance to the fourth point. All these features were present in the sections of the three reported cases. All these cases belong to the gummatous group of the type.

The clinical picture in the first case is also interesting for here is another case of a cardiac

catastrophe producing signs and symptoms of an 'acute abdomen'.

SUMMARY

Three cases of multiple gummata of the heart are reported. They all showed involvement of the left ventricular wall and the interventricular septum in a gummatous process. One of them also showed an aneurysmal dilatation of the left ventricle.

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A REPORT OF TWO CASES OF KALA-AZAR WITH DELIRIUM AS A PROMINENT FEATURE

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ONE point that is particularly stressed in every book on tropical diseases is the absence or extreme rarity of mental symptoms like delirium, mental drowsiness, etc., in kala-azar. This is one of the few negative points of diagnostic significance in clinical medicine.

Even in 'enteric type' of the disease, though the case may simulate one of enteric fever very closely, the toxic drowsiness of the enteric patient is conspicuous by its absence. Even in what Manson-Bahr terms the 'acute toxic' type with very high mortality mental symptoms are singularly absent.

The following two cases of kala-azar from the wards of the General Hospital, Madras, proved by the demonstration of Leishman-Donovan bodies in the sternal marrow, showed delirium as a very striking feature and the resemblance to enteric fever, especially in the first case was so great that every possible measure was made use of to make absolutely certain that these were not cases of kala-azar with enteric fever as in the case reported by Piccinelli: He was treating an adult of 24 years for typhoid fever (proved by blood culture) when a blood film examination revealed several groups of Leishman-Donovan bodies and the diagnosis of kala-azar was confirmed by spleen

puncture. Meningitis complicating kala-azar was also excluded in these cases by a thorough investigation of the cerebrospinal fluid.

Case 1

The patient, R., was admitted on 15th April, 1948, for continuous fever of one month's duration. The fever was insidious in onset and was more or less continuous up till the time of admission. He was being treated with quinine mixture in Police Hospital, with no benefit. Frontal headache. No sleep at nights. Urine highly coloured. No previous history of similar complaint. History of malarial attack 7 to 8 years ago which responded to quinine sulphate mixture.

Examination revealed the patient to be a well-nourished individual, not very ill, well oriented. Tongue heavily coated in the centre. Not jaundiced. No palpable lymph glands. Temperature 103°F.

Flatulent distension of abdomen present. Spleen palpable for $\frac{1}{2}$ inch below costal margin, firm, rounded antr. border. Liver not palpable. Respiratory and cardiovascular systems normal. Pulse 108 per minute, regular, volume and tension good. Blood pressure 100/70 mm. Hg.

C.N.S.—No neck rigidity or Kernig's or Brudzinski's signs. Cranial nerves, motor and sensory systems normal.

Investigations.—Urine: sp. gr. 1012, neutral. No albumin or sugar or urobilinogen or bile pigments.

R.B.C. 3.7 mil. per c.mm.

Hb. 75 per cent normocytic picture. No malarial parasite in blood smear. Napier's Aldehyde test and Chopra's test were negative.

W.B.C. 2,000 per c.mm., polymorphs 44 per cent, lymphocytes 35 per cent, monocytes 20 per cent, eosinophils 1 per cent. The case at this stage looked like one of enteric fever and was getting treated accordingly. The temperature was remittent with a maximum of 103 and a minimum of 101, the highest temperature being reached at about 12 p.m. and the lowest at about 8 a.m.

19th April, 1948.—The patient was very delirious and developed neck rigidity. Lumbar puncture was done. C.S.F. clear not under pressure. Proteins 60 mg. per cent, globulin in negative, chlorine 700 mg. per cent, sugar 53 mg. per cent, no cells, culture for enteric group of organisms negative. Flatulent distension of abdomen and retention of urine present. Widal reaction was negative and blood culture for enteric group of organisms and urine culture were sterile. Sternal puncture was done and the marrow was sent for culture for enteric group of organisms. Leishman-Donovan bodies were identified in the marrow. Sternal marrow culture for enteric group of organisms negative.

20th April, 1948.—Patient exhausted. Still disoriented. Temperature 101.6°F.

21st April, 1948.—Stibatin given intramuscularly (200 mg.).

22nd April, 1948.—Temperature 102°F. Patient still disoriented and incoherent in talk.

23rd April, 1948.—Urea stibamine given, 0.05 gm. intravenously. Abdomen still distended. Bladder distended up to midway between symphysis and umbilicus. Patient still disoriented.

24th April, 1948.—Temperature normal, flatulence better, passed urine freely. Mental process quite normal.

25th April, 1948.—Temperature normal, urea stibamine 0.05 gm. intravenously. The further convalescence was uneventful and the patient was discharged after a full course of urea stibamine.

Case 2

The second patient, I., came in on 2nd October, 1947, with a history of more or less continuous fever of 17 days' duration which was insidious in onset. The fever used to range from 100°F. in the mornings to 102°F. or 103°F. at nights. The patient was able to get about his normal work without inconvenience. Four days before admission he felt very weak after returning from the work and soon became unconscious. He was in this stage for 1 to 2 hours and then was found to be disoriented and incoherent in his talk. Examination revealed a well-nourished individual, delirious, picking at the bed clothes, tongue moist and clean, no palpable lymph glands.

Cardiovascular and respiratory systems normal.

Abdomen not distended, liver and spleen not palpable, no neck rigidity or Kernig's or Brudzinski's sign, motor and sensory systems normal.

Investigations.—Urine : sp. gr. 1018, acid, no albumin, sugar, bile or urobilinogen.

W.B.C. 3,800, polymorphs 63 per cent, lymphocytes 27 per cent, eosinophils 4 per cent, monocytes 1 per cent. No malarial parasite in peripheral blood smear. The case was admitted in the Enteric Ward and was getting a simple diaphoretic mixture. Blood was sent for Widal reaction and also for culture for enteric group of organisms. Urine and motion were also sent for culture. As the patient was very delirious, lumbar puncture was done. The cerebrospinal fluid was not under tension. Proteins 10 mg. per cent, chlorides 610 mg. per cent, sugar 53 mg. per cent, no cells, culture sterile. The temperature was ranging between 101°F. and 99°F. On 8th October, 1947, sternal puncture was done and the marrow sent for culture for enteric group of organisms was reported as sterile. Leishman-Donovan bodies were detected in the marrow. The patient was put on stibatin intramuscularly daily (200 mg.). On 10th October, the temperature was normal and the patient was quite well-oriented and mentally quite clear. The

further course was uneventful with a normal temperature and the patient was discharged after a full course of stibatin.

I tender my grateful thanks to Dr. A. Srinivasan, M.R.C.P. (Lond.), Honorary Physician, Government General Hospital, Madras, for kindly going through these case reports and the Superintendent, General Hospital, Madras, and the Surgeon-General with the Government of Madras, for permission to report these cases from the General Hospital.

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TREATMENT OF KALA-AZAR WITH PENTAMIDINE ISOTHIONATE

A STUDY OF 55 CASES

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PENTAMIDINE isothionate or 4:4'-diaminodiphenoxypentane is one of the aromatic diamidines synthesized by Ewins and has been used for the treatment of visceral leishmaniasis by different workers. 4:4'-diamidinostilbene or stilbamidine, another member of the diamidine group of drugs, was also successfully used for the treatment of kala-azar; but this drug has now been withdrawn from the market, perhaps because of the peculiar neurological sequelae developing after its use in many cases. Pentamidine isothionate is the only drug available now for the treatment of such kala-azar cases as have proved resistant to antimony. This article is based on a study of 55 cases treated with this drug. All the patients were admitted into the Civil Hospital, Sibsagar (Assam), under the care of the writer.

Patients and treatment

Sex.—Male 31, female 24.

Age.—There were 2 cases between 1 and 5 years, 10 between 6 and 10 years, 17 between 11 and 15 years, and the remaining 26 cases were above 16 years.

Race and occupation.—All the patients were Assamese cultivators.

Duration of disease.—This varied from 2 to 12 months but a few went beyond this period.

Previous treatment.—Thirty-four casts were antimony resistant and 21 were antimony non-resistant. A case was regarded as antimony resistant if no improvement was seen after 10 or more injections of urea stibamine. A case that did not receive any injection of urea stibamine or had less than 10 injections of the drug was taken as antimony non-resistant.

Diagnosis.—Every case on admission was examined clinically and aldehyde test was done as a routine measure. Spleen puncture was done in every suspected case and the smear was examined for L.D. bodies. Diagnosis of all the cases included in this investigation has been confirmed by the demonstration of L.D. bodies in the spleen puncture material.

Treatment.—The patients after admission were kept in the hospital for about a week before the specific treatment was given. This period was utilized for necessary examinations and proper investigation of the cases. This also helped them to adjust themselves to conditions in the hospital. The patients were generally given the hospital full diet which consisted of rice, dal, vegetables, milk every day and fish or meat twice weekly, unless contra-indicated by intestinal troubles or very high fever. Moderate fever and disinclination for food were not considered to be sufficient reasons for curtailment of full diet. Usually with a little persuasion the patients could be induced to take the above diet. The patients were usually given a mixture containing quinine during the period of investigation to eradicate any possible infection with malaria. During the period of treatment with the specific drug they were given an iron mixture. Associated diseases such as ankylostomiasis, amœbiasis, etc., were treated after the course was finished. Complications such as dysentery and diarrhoea, if not severe, were treated along with the course of the specific treatment; if severe, these were treated and arrested before it was started.

Dosage.—The drug is supplied in 10 per cent solution so that one cc. of the solution contains 100 mg. of the drug. No fixed dose was given to every patient. The maximum single dose was calculated on the basis of weight. To test the reaction of the patient to the drug and also to increase the tolerance of the patient the first two injections were usually given with a dose smaller than the calculated maximum, and the maximum dose was given in all the injections thereafter. The injections were given daily. The maximum single dose and the total number of injections given to a patient varied. Table I shows the dosage employed in these cases.

TABLE I

Maximum single dose per lb. of body weight	NUMBER OF CASES		
	Antimony resistant	Antimony non-resistant	Total
0.75 mg. ..	1	0	1
1.0 " ..	11	8	19
1.5 " ..	20	12	32
2.0 " ..	2	1	3
TOTAL ..	34	21	55

No distinction was made as regards dosage between the two groups of cases. The number of injections to each patient varied from 10 to 20. The relative total dosage calculated per 100 lb. of body weight received by the patients ranged from 0.60 to 3 gm.

Methods of administration.—Twenty-five patients received the drug intravenously, 28 intramuscularly and 2 patients received the first few injections intravenously and later ones intramuscularly. The purpose of giving the drug intravenously to some and intramuscularly to others was to see whether both methods were equally effective.

Reactions.—When the drug was given intravenously almost all complained immediately after injection of a sensation of burning and tingling all over the body, a feeling of tightness over the chest and epigastric pain. They showed a tendency to cough, there was flushing of the face and the pulse was slightly accelerated. These manifestations were mild and did not give any cause for alarm and subsided within a minute or two. These mild reactions were most noticeable during the first three or four injections and generally the latter injections were without any symptom. Only in one case (case 15) was a severe reaction noticed.

A female, aged 20 years, weighing 70 lb., was given the 1st injection of 0.2 cc. intravenously on 8th April, 1947, and 2nd and 3rd injections of 0.7 and 1 cc. respectively on the following two days. She did not show any reaction except a slight burning sensation all over the body. She was given the 4th injection of 1 cc. on 11th April, 1947, and immediately after it she developed a severe reaction with dyspnoea, severe burning sensation all over the body, a sense of impending death, imperceptible radial pulse and fits of cough. She got almost immediate relief after an injection of $\frac{1}{2}$ cc. of adrenaline. The subsequent injections of 1 cc. were practically without any reaction.

The intramuscular injections were painless and did not cause any reaction.

Toxicity.—One case (case 5) developed general anasarca towards the end of the course. Three cases (cases 15, 26 and 43) developed œdema of

this stage bladder symptoms become very marked and the patient passes very agonizing and painful days with constant dysuria, frequent hæmaturia and pyuria, and rapidly loses ground.

Dukes' present classification like the one he propounded in neoplasm of the rectum is interesting and at the same time practical and certainly better than the ones mentioned in pathological textbooks, the caseous type, the cavitory type, the cretaceous type and the miliary type. In my small series, 4 cases were in stage IV and 3 in stage III.

Age incidence.—The average age incidence was twenty-nine, the youngest being 18 and the oldest 39. This is in keeping with the figures of other observers and it may be said that tuberculosis of the kidney is a disease of the 2nd, 3rd and 4th decades of life and is uncommon in the very young or the very old.

Sex.—Five cases were in males and two in females.

History.—The longest history was 7 years. This was a case whom I had admitted previously in the hospital 4 years ago for the same condition and the surgeon under whose care he was at the time had deemed operative interference too hazardous and not advisable in view of the affection in his lungs. He came to me again early last year complaining of incessant polyuria, unbearable dysuria and frequent hæmaturia, and begging that something should be done to give him relief. Almost against my will and thinking that I could not do much harm and may do some good, I decided to remove his kidney and ureter. He had proliferative lesions in his right lung and now requires thoracoplasty to cure him.

The shortest history is in the case that is at present under my care, an Anglo-Indian sergeant in the Calcutta Police whose history dates back only to last October. Previous to this he was asymptomatic and did his full duties.

Symptoms.—The usual symptoms that brought the patients to the hospital were dysuria, polyuria, hæmaturia, fever, renal pain, general deterioration of health and loss of weight. It is very difficult to say what is the earliest symptom, probably nocturnal polyuria and slight evening rise of temperature but surgeons usually do not see these cases until dysuria and pain become marked. Early hæmaturia may bring the patient quickly to the surgeons' notice. In my last case pain of colicky nature was the main presenting symptom and a provisional diagnosis of renal calculus had been previously made. This was supplemented by the presence of a small dense shadow in the kidney region, obviously a calcareous spot in the kidney.

Investigations.—All routine examinations were made. In four cases tubercle bacillus was demonstrated in the urine after centrifugalization and staining. Animal inoculation was not

considered feasible in view of the long delay required for such examination. Intravenous pyelography was done in all the cases and revealed various pyelographic appearances from total non-excretion to abnormal appearances of the calyces or to hydronephrosis. Cystoscopy was done in all the cases except the last one. Almost in every case the bladder showed evidences of chronic cystitis, engorgement and œdema. Ureteric catheterization and retrograde pyelography were possible in only two cases.

Operation.—In all the cases except one, the writer has extirpated the diseased kidney together with almost the whole of the ureter (figures 5 and 6, plate XV). He put the patient on his back in the beginning, made a 3-inch midline suprapubic incision, isolated, ligated and divided the ureter as close to the bladder as possible. Then the patient was turned on his side and after the kidney pedicle was divided and secured, finger separation brought the whole of the ureter out together with kidney. The importance of removal of the ureter together with the kidney is nowadays being widely stressed and seeing that all the cases belonged to stage IV or late stage III it seemed very necessary.

Post-operative period.—A troublesome post-operative complication that occurred in three of the cases and is in course of occurring in another is the slow breaking down of the wound, starting at about the 12th, 13th or 14th day. In all the cases the wound seemed to heal without trouble and only after the stitches had been taken out slight serous discharge and slow gaping became evident and continued for a long time. In a particularly serious case (figure 5, plate XV) practically the whole of the incision line gave way, the muscles seemed to fall apart and one was looking into a deep hole. The patient began to run slight temperature, granulation tissue was very slow in growing and progress was almost at a stand still. The patient seemed on the downward path. Many drugs including penicillin were tried without the slightest response.

At this time he was given a course of streptomycin and the response even after the first gramme was very pleasing. The fever quickly responded and the refractory wound quickly showed signs of healing. The course of streptomycin had to be repeated twice or thrice and in the writer's opinion made the essential difference between recovery and death. This particular complication has been happening so constantly in the last few cases and the beneficial response with streptomycin has been so marked that the writer now intends in his next series of cases to administer the drug from the beginning of the post-operative period as a prophylactic measure.

Results.—There has been no mortality in these 7 cases; five of them have markedly improved. Two have gone back to work. One case who is an employee of the Calcutta Fire

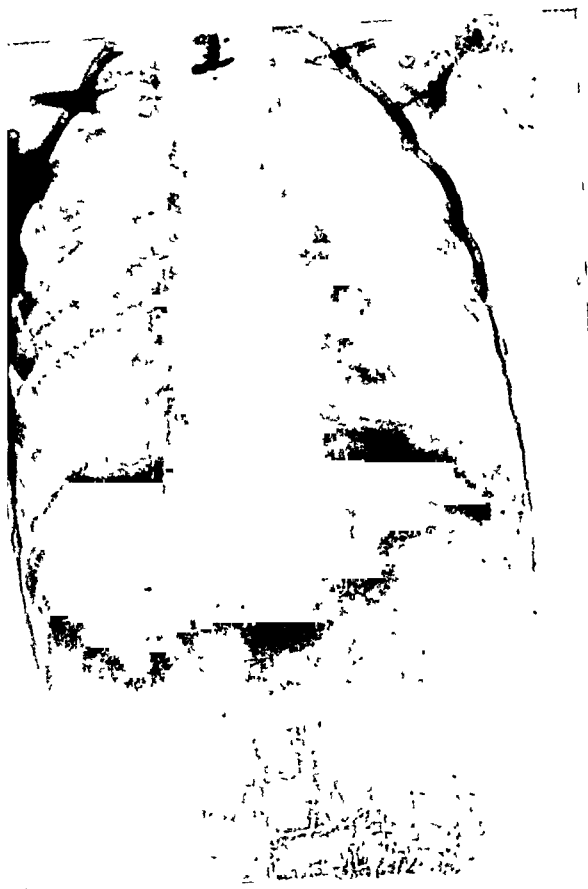


Fig 1



Fig 2



Fig 3



Fig. 4.



Fig. 5.



Fig. 6.



Fig. 7.



Fig. 8.



Fig. 1.—Gumma of the heart from case 1.

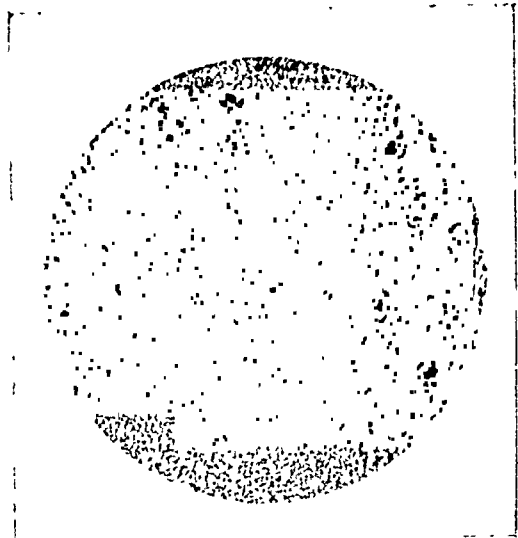


Fig. 2.—H & E Stain $\times 150$ from case 1.

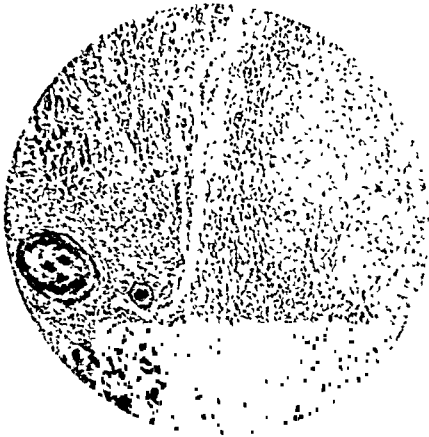
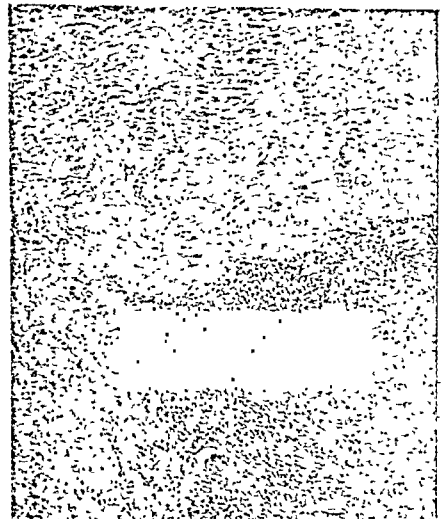


Fig. 3.—H. & E. Stain $\times 150$ from case 1.



Fig. 4.—Gumma of the heart from case 1.



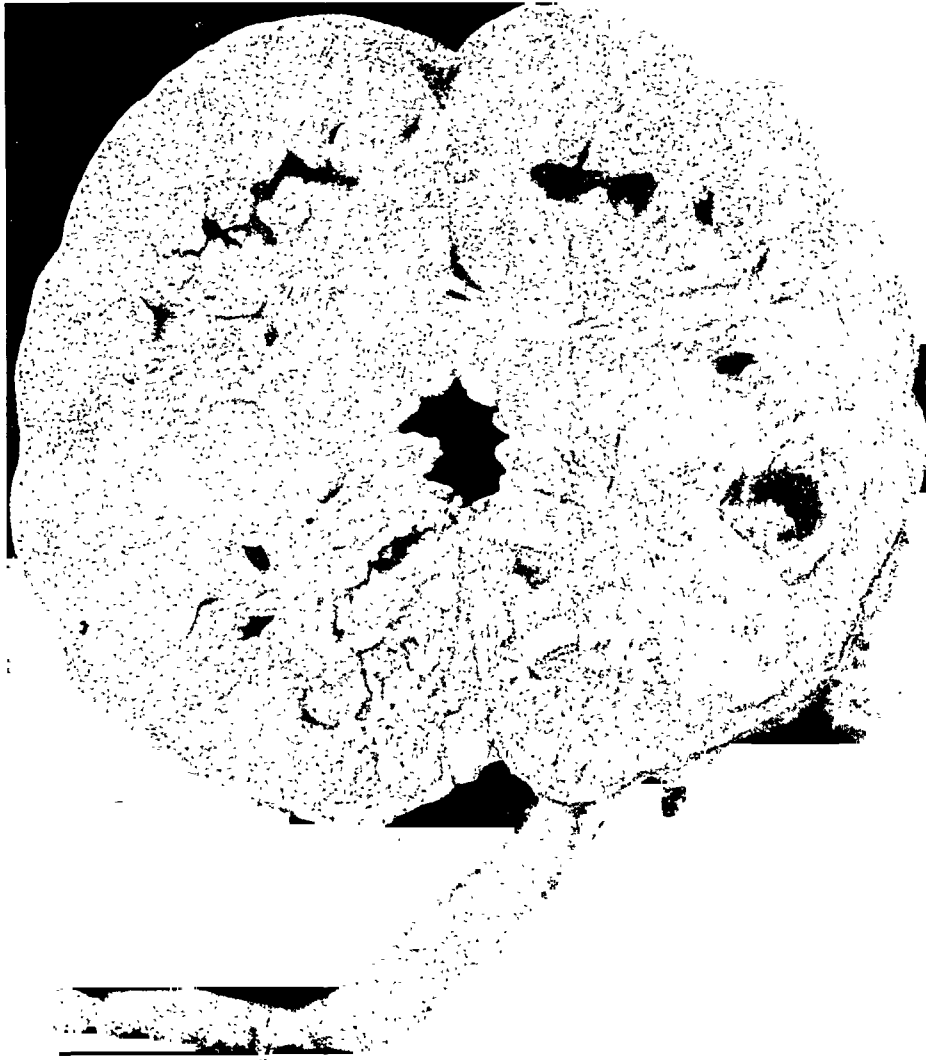


Fig. 5.—Showing ulceration, caseation and cavitation of the kidney.
The ureter is thickened.



Brigade has started his duties. The man with the worst kidney and lesion in his lung has been keeping good health and now has no urinary symptoms. He passes urine 5 or 6 times a day and has undisturbed sleep at night. One case, youngest, has, I am told, not been keeping well and still has frequency and dysuria.

Summary

1. The life history of tuberculous disease of the kidney and its surgical treatment as judged from a small series of cases is presented.

2. Cuthbert Dukes' views as regards the pathology of the disease are mentioned.

3. An important post-operative finding, *viz.*, late and gradual disruption of the wound, is discussed and its rapid response to streptomycin is stressed.

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TWO CASES OF AMÆBIC LIVER ABSCESS WITH COMPLICATIONS

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AMÆBIC abscess of the liver when not properly treated tends to increase in size and often ruptures into the adjacent tissues, *viz.*, lung, pleura, peritoneum, pericardium or abdominal wall, and less commonly into the stomach, duodenum or hepatic flexure. An effusion may occur into the pleural or peritoneal cavities as a result of direct spread of the inflammation from the advancing abscess. Abscess in the lung may result from extension of inflammation through the diaphragm or as a metastatic condition. Amœbic abscesses have also been observed in brain and spleen. Two cases that illustrate some of the important complications of an amœbic abscess of the liver are described below.

Case reports : Case 1

The patient was admitted to hospital on the 14th July, 1942, with a complaint of pain in the abdomen. He was operated upon for perinephric abscess on 19th July, 1942. No pus was found and the wound closed. On 29th July, 1942, he showed a cystic swelling in the lower abdomen, extending up to within 1 inch of the umbilicus. His total leucocytic count was 14,800 per c.mm. with polymorphs 82.0 per cent. A diagnosis of pelvic abscess was made and the patient was operated upon on 30th July, 1942. Two pints of pus were evacuated. There was some improvement in his general condition. The total leucocytic count came down to 9,000 per c.mm. and polymorphs to 66.0 per cent. He died on 16th August, 1942.

Post-mortem findings.—Both the paracolic gutters showed free purulent fluid. The cæcum,

ascending colon and descending colon were slightly adherent to the posterior abdominal wall. The liver showed adhesions to the diaphragm at its upper surface and to the lesser curvature at its posterior surface. Left lobe showed an abscess, 3 inches by 1 inch, at its posterior surface. Contents of the abscess consisted of necrotic tissue and its wall was shaggy. The cæcum and ascending colon showed no ulceration. The descending colon was slightly atrophied, adherent to the posterior abdominal wall and its upper part showed a few ostia slightly larger than pin-points in size. Depth of these ostia appeared to be up to the thickness of the mucosa only and there was no undermining of the edges of these ostia.

Histopathology : (1) *Large intestine.*—The pin-point ostia referred to above were tiny amœbic ulcers. They were most marked on the splenic flexure in which relatively large number of parasites were observed. The mucous membrane was less affected than the deeper layers and much of the muscle had been replaced by fibrous tissue infiltrated with chronic inflammatory cells.

(2) *Liver.*—The lesion was typical of an amœbic abscess except that no amœbæ could be identified in the sections examined. The abscess cavity was lined by a shaggy layer of pink-stained, acellular and structureless material representing necrotic liver tissue. Outside this was a well-marked zone of lymphocytes and a few plasma cells and monocytes. Polymorphs were conspicuous by their absence. Just beyond this was a broad indefinite layer of compressed liver tissue in which the lobular arrangement had been lost and the columns of hepatic cells had become broken up into groups of 1, 2 or 3 cells undergoing degeneration, the cells being swollen, rounded and with karyolysis and vacuolation of the cytoplasm. This area was permeated by a variable number of chronic inflammatory cells. The chronicity of the lesion was shown by areas of collapse and fibrosis in which the small bile ducts had survived though the polyhedral cells had been destroyed rather like the appearance in sub-acute yellow atrophy. The surrounding liver had normal architecture but the portal tracts showed round-celled infiltration, the capillary sinuses were congested: the liver cells showed cloudy swelling and the Kupffer cells were loaded with minute granules of dark brown pigment (old malarial pigment).

(3) *Lung.*—An abscess was present. The wall of the abscess consisted of pink-staining necrotic debris centrally. Outside this was a zone in which the architecture of the affected lung could just be distinguished. The blood vessels and bronchioles had survived longer than the more delicate alveoli, and throughout this zone were very large number of amœbæ containing granules, vacuoles, RBC's and altered blood pigment. Beyond this was a broad zone of

pneumonia and large number of polymorphs indicating secondary bacterial invasion.

Case 2

This case was received as a transfer from another hospital where he had been given 8 injections of emetine for dysentery diagnosed as amœbic in nature. He was coughing up chocolate-coloured and foul-smelling sputum on admission. Neither sputum nor stools showed amœbæ. Emetine was continued. He made no improvement and died 24 days after admission.

Post-mortem findings.—The liver showed an abscess cavity 1 inch by 1 inch on the upper surface of the right lobe. Abscess was walled in by fibrous tissue and the surface of the liver was adherent to the diaphragm which was thin and dark in colour at the side of contact with the abscess. Contents of the abscess cavity consisted of thick creamy pus. Smears from the pus showed necrotic liver cells, mononuclears, a fair number of polymorphs and RBC's. Culture of pus was sterile. The peritoneal cavity showed sero-purulent exudate in paracolic grooves and in retrovesical pouch. Smears from the exudate showed pus cells in fair number. Gram-negative coliform bacilli and staphylococci were also present in the exudate. Capsule of the spleen was thickened on the diaphragmatic surface, and was adherent to the diaphragm and showed an abscess 1 inch by $\frac{1}{2}$ inch in size. Contents of this abscess were similar to those of the abscess in the liver. Lower lobe of the right lung was adherent to the diaphragm and its base showed an abscess which involved nearly the whole of it. The anterior end of the posterior horn of the lateral cerebral ventricle and the middle of the corona radiata showed pus slightly greenish in colour. Smears showed pus cells in large numbers and Gram-negative coliform bacilli and staphylococci as were seen in the exudate in the peritoneal cavity.

Histopathology.—The liver showed a thick, fibrous and almost structureless wall of an old abscess cavity. Inside the wall were degenerated liver cells, polymorphs and mononuclears. No amœbæ or any other organisms were seen. The liver tissue on the periphery and away from the abscess cavity was normal. Lower lobe of the right lung showed abscess cavity formation and much infection with Gram-positive cocci. Alveoli on the periphery of the abscess showed broncho-pneumonia. No amœbæ seen. The brain showed a small abscess with necrotic debris and cells consisting mainly of fibroblasts, histiocytes and a few polymorphs.

Comments

It is proposed to offer comments on some special features only.

Previous history of amœbic dysentery.—Case 1 gave no history of amœbic dysentery. Previous history is available in most of the cases that

show liver abscess during life or on the autopsy table but cases that do not give a previous history have been reported by a number of workers including Rogers (1921) who observed that 20 per cent of his autopsy cases of liver abscess had no history of amœbic dysentery although amœbic ulcers were present in the intestines.

Amœbic ulcers in the intestines.—Ulceration was confined to the upper part of the descending colon only in case 1. This is a rather uncommon site for amœbic ulceration. Localization of ulceration to the upper part of the descending colon was very probably responsible for the location of the abscess in the liver on the posterior surface of the left lobe in this case. Amœbæ from the ulcers on the splenic flexure were most likely to be carried by the blood stream to the left lobe of the liver as has been suggested by Fairley (1932, 1933) on the basis of experimental work on dogs by Copher and Dick (1928). Absence of intestinal manifestations has been explained by Rogers (1921) and other workers as due to localization of the ulcers to the upper part of the colon. Though ulceration was present in this case in the descending colon but it did not lead to clinical symptoms of amœbic dysentery or the symptoms caused were so mild that the patient did not consider them significant. Case 2 showed no ulceration of the intestines though a couple of weeks before his death he was diagnosed as a case of amœbic dysentery. Ulcers had obviously healed on treatment without leaving any evident scar. Amœbic ulcers vary in size from minute ulcers that are visible under the microscope to extensive ulcers involving all the coats of the bowels. Microscopic lesions may heal without leaving any obvious scar but amœbæ may still be found in the deeper tissues as is suggested by the experimental work of Hoare (1925) on kittens. He infected them artificially with *Entamoeba histolytica* and killed them 6 weeks after infection. Microscopic examination of the sections of the intestines showed amœbæ at the base of the mucous membrane though there were no naked-eye lesions.

Abscess in the liver.—Contents of the abscess in case 2 were yellowish in colour. This was obviously due to secondary bacterial infection which might have taken place before the patient was put on emetine. The wall of this abscess consisted of thick fibrous tissue which was smooth on its inner surface. MacCallum (1929) attributed encystment to the development of another abscess in the liver or elsewhere. The explanation given by Rogers (1921) for the encystment of liver abscess, however, is more consistent with the history of the case. He considered this to be a result of treatment. Amœbæ could not be demonstrated in this case as they disappear from an abscess which is secondarily infected with bacteria or becomes encysted. Failure to see amœbæ in the liver abscess in

case 1 could be explained by supposing that they were absent in the tissue examined and that serial sections would have shown amœbæ.

Condition of the surrounding liver tissue.—It was normal in case 2 where the patient was on emetine for some time before he died. The surrounding liver tissue in case 1 had normal architecture but the portal tracts showed round-celled infiltration outside the broad zone which presented a histological appearance similar to that of subacute yellow atrophy of the liver. The liver cells showed cloudy swelling and the Kupffer cells were loaded with minute granules of dark brown pigment. Karunaratne (1940) considered round-celled infiltration of the portal tracts as the earliest stage in the development of a true cirrhosis on the basis of experimental work as well as autopsy findings. He observed round-celled infiltration of the portal tracts during routine post-mortem work in Colombo in a variety of conditions including some acute infectious fevers and ankylostomiasis in children where the ætiology of its causation was obscure. As round-celled infiltration as well as degeneration or necrosis of the cells developed as a result of metabolic toxins, bacterial toxins, chemical poisons and amœbic toxins, he was of opinion that the ætiology of this pathological change was not necessarily amœbic.

Abscess in the lung, brain and spleen.—Both cases showed abscess in the right lung. Amœbæ could be seen in the lung abscess in case 1 only. Case 2 showed abscess in the brain and spleen also. The abscess in the brain was secondarily infected with bacteria and no amœbæ could be demonstrated. Abscess in the brain secondary to amœbiasis is not a common condition. Karunaratne (1940) observed that 52 cases only had been recorded till that time and amœbæ could be demonstrated in only 10 of the reported cases. Kartulis whose work has been referred to by Karunaratne (1940) however, observed amœbic cerebral abscesses in 3 per cent of all cases with abscess in the liver. The abscess in the spleen was smaller than the abscess in the liver and was similarly encysted. No amœbæ were demonstrated. Abscess in the spleen is a much rarer complication than cerebral abscess.

Summary

The post-mortem findings of two cases of amœbic liver abscess with complications are described. Case 1 had no history of amœbic dysentery. The abscess in the liver was situated on the posterior aspect of the left lobe. Pin-point amœbic ulcers were found in the upper part of the descending colon only. The liver showed a typical amœbic abscess but amœbæ could not be demonstrated in histological sections. The abscess in the lung as well as the pin-point ulcers in the descending colon showed amœbæ in large numbers. Case 2 was admitted to hospital with amœbic dysentery. At autopsy

no dysenteric ulceration of the gut was to be seen. He had an encysted liver abscess as well as an encysted abscess of the spleen, abscess of the lung and a cerebral abscess showing secondary infection. No amœbæ could be demonstrated in any of the abscesses.

I am much indebted to Dr. W. A. E. Karunaratne, Professor of Pathology, Ceylon Medical College, Colombo, for his advice and suggestions in the writing of this paper.

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EXCRETION OF NICOTINIC ACID IN NORMAL HEALTHY HUMAN BEINGS

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Introduction

ESTIMATION of nicotinic acid in biological fluids has not yet proved to be of value in diagnosis or treatment of any case wherein the clinical symptoms may reveal a gross deficiency of the members of the B complex group. This may be due to the fact that there is a very great variation in the amount of nicotinic acid excreted. Recently a view has also been advanced that nicotinic acid may be synthesized in the biological system. There may be a great variation in one's capacity to synthesize nicotinic acid which leads to variations in the amount excreted. Attention has, however, been directed in the present cases to determine the amount excreted normally by healthy individuals and also after a test dose, to add to the data already existing on the subject. Moreover, the cases include persons who live on almost a balanced diet, i.e. persons who take both rice and wheat and vegetables, etc., in contrast to the cases studied by Swaminathan and Giri which included rice-eating individuals and Kochhar whose cases were drawn from wheat-eating population. Cases studied by the above workers were rather few in number. In the present investigation 44 cases were studied.

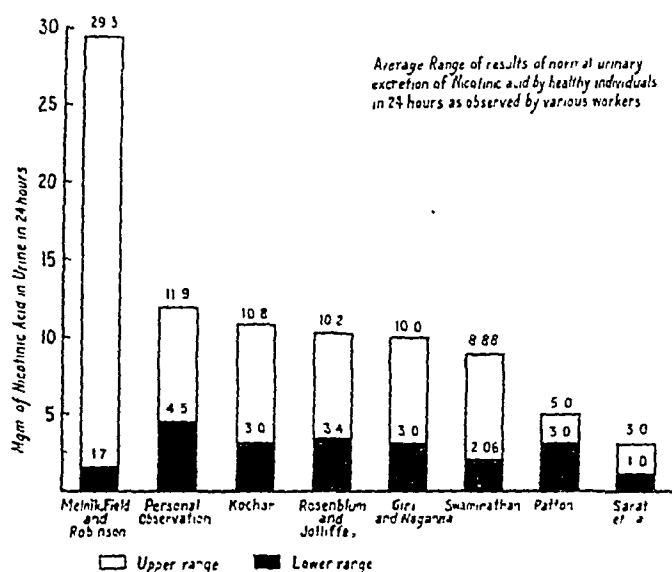
Experimental technique

For the estimation of nicotinic acid in urine aniline cyanogen-bromide method was adopted. Estimations were carried out in 24-hour collection on urine under normal conditions. Then in the same individual 50 mg. of nicotinic acid were administered intramuscularly and excretion estimated as before. The results are shown in the graphs (personal observation).

Discussion

Although there is an individual variation in the amount of nicotinic acid excreted normally by healthy individuals, there is a close similarity in the results obtained by various workers making the range limited. Giri and Naganna found the range to vary from 3 to 10 mg. His observations were made on South Indians who are mainly rice eaters. Kochhar found the range to be 3 to 10.8 mg. among his normal cases who belonged to Punjab an essentially wheat-eating province. In the present case observations were made among adults (both males and females) who eat both rice and wheat and represent an average Indian diet eaters, excretion of nicotinic acid varied from 4.5 to 11.9. The results of Rosenheim are also practically in the same range, viz. 3.4 to 10.2 (figure 1). The higher results (1.7 to 29.3) obtained by Melnick *et al.* are attributed by the authors themselves to the non-specificity of the method employed and they believe their range to be nearer to the lower value. The lower results achieved by Datton (3.0 to 5.0) and Sarat (1.0 to 3.0) are also due to defective technique employed.

Fig. 1.

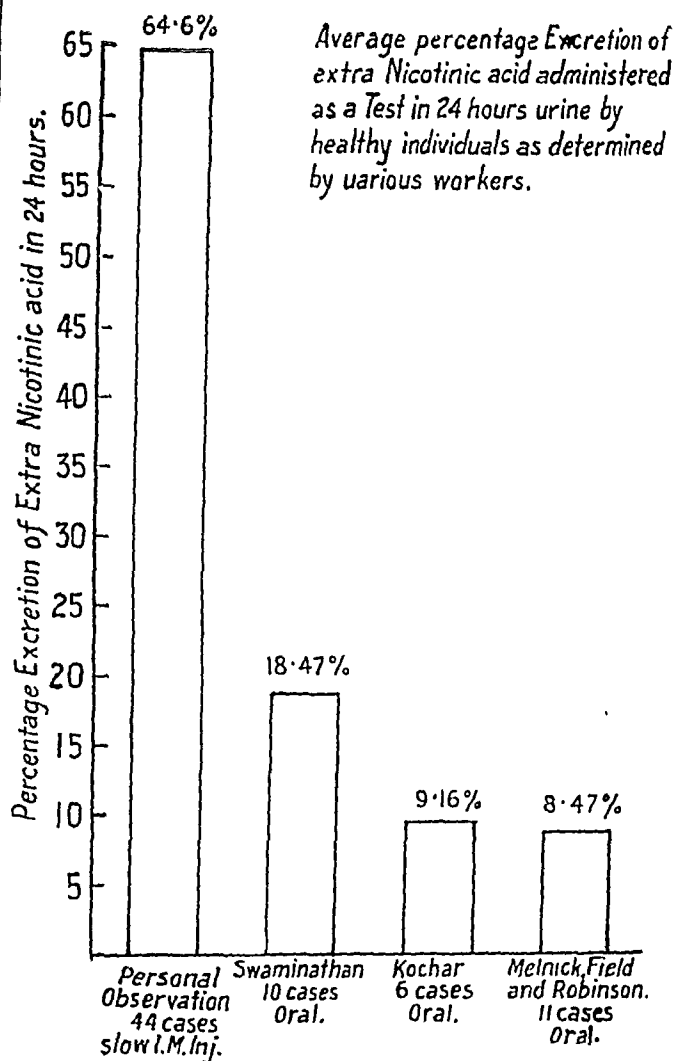


The range given by Swaminathan (2.06 to 8.88) is very well covered by the ranges given by Giri and Kochhar and the observations made in the present work. His higher range was less probably because he was mostly dealing with pre-eminently rice-eating population.

It can, therefore, be concluded that the amount of nicotinic acid excreted in 24 hours by normal healthy individuals varies from 2 to 12 mg.

It has been suggested by Melnick *et al.* that the percentage excretion of the test dose varies directly with the size of the dose. This conclusion is corroborated by the results of Kochhar, Giri and Swaminathan. A very large amount is excreted when the drug is administered intramuscularly as compared with oral administration. The average percentage excretion after an oral administration of the drug has been found by Kochhar to be 9.16, by Swaminathan 13.47 and by Melnick 8.47, whereas in the present case an average percentage excretion of 64.6 has been obtained after an intramuscular administration of nicotinic acid (figure 2).

Fig. 2.



Summary

1. An investigation of the urinary excretion of nicotinic acid has been carried out on 44 normal individuals.
2. The initial excretion of nicotinic acid in urine in 24 hours ranges between 4.5 and 11.9 mg.
3. The average percentage of nicotinic acid excreted after an intramuscular injection of 50 mg. of nicotinic acid is 64.6 per cent.

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SEROLOGICAL TECHNIQUE (contd.)

IMMUNOTHERAPY

By S. D. S. GREVAL

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IMMUNIZATION WITH TOXOIDS

BESIDES diphtheria, already dealt with, immunity against staphylococcus infections, tetanus and gas gangrene is now produced with toxoids. So far there are no tests corresponding to the Dick test and Schick test for testing susceptibility to staphylococcus infection. The question of susceptibility hardly arises in case of tetanus and gas gangrene : all involved are as a rule susceptible.

STAPHYLOCOCCUS INFECTIONS

Toxoid.—It is a filtrate of a liquid culture of staphylococci rendered innocuous by formol like the diphtheria toxoid. The toxin is no longer hæmolytic, dermo-necrotic or lethal to laboratory animals. Unlike the scarlatinal toxin the filtrate loses only toxicity not antigenic power. Ampoules ready for use are available commercially. Staphylococcus Toxoid B is the undiluted toxoid and Staphylococcus Toxoid A is a 1 in 10 dilution. An exact standardization like the one in diphtheria is not possible.

Dose.—A beginning is made with 0.5 cc. of a 1 in 10 dilution, given intramuscularly. If the reaction is negligible, a course of the undiluted liquid is given, beginning with 0.1 cc. and increasing by 0.1 cc., every 4 to 7 days, until 1 cc. is reached. If a local or general reaction occurs, the next dose is not increased. A short interval is to be preferred to a long one in the absence of a reaction.

Results.—The toxoid is more useful than vaccine in skin infections. The immunity, however, is short-lived. Those susceptible to such infections should receive a few injections every year.

The toxoid is also used in the active treatment of boils and carbuncles. A course of injection is begun and the boils are aborted. In such a line of treatment penicillin may be combined with the toxoid.

TETANUS

Toxoid.—It is a filtrate of a liquid culture of *Clostridium tetani* rendered atoxic by formol. An exact standardization is possible : (1) The toxin is prepared and standardized in the usual way, and bottled. (2) To each bottle of toxin is added 40 per cent formol to give a final concentration of 0.3 per cent, and the bottles incubated for 22 days. (3) Guinea-pigs (330–380 grammes) are injected with 10 cc. of the fluid (on both sides of the abdomen) and observed for 25 days. They are weighed on the 5th, 10th, 20th and 25th day. Spastic paralysis is looked for. If signs of tetanus develop, the bottles are incubated for a few more days and tested again. (4) Approved fluid is preserved with 10 per cent 'merthiolate' to get a final concentration of 0.01 per cent.

Dose.—1st dose of 1 cc. (given subcutaneously) is followed 8 weeks later by a second dose of 1 cc. Then a dose of 1 cc. is given 8-monthly or 12-monthly.

Results.—The immunity even without the 8-monthly or 12-monthly doses is of a high order. It has been recommended that all children, farmers and workmen who are exposed to injuries which might lead to tetanus should be immunized. During World War II the Forces were immunized. British wounded soldiers received antitoxin as well but American wounded soldiers received only a boosting dose of the toxoid. Indian wounded soldiers were given the antiserum in case of severe injury only. Cases of tetanus occurring in the immunized men were relatively mild although they had a short incubation period. When treated with antitoxin they had a low mortality rate. Previous administration of tetanus antitoxin does not interfere with the active immunization with the toxoid.

Reaction.—Allergic subjects may develop a reaction, due to the broth in which the culture is grown. For them the 1st dose may be 0.1 cc. followed, the next day, by the usual dose of 1 cc. Adrenalin controls the reaction.

Combined active and passive immunization.—Injections of the antitoxin serum and of the 1st dose of the toxoid may be given at the same time after an injury and exposure to tetanus. The toxoid commenced 4 weeks after the last dose of the serum, however, is supposed to produce better immunity.

GAS GANGRENE

Toxoid.—Toxoid from cultures of *Clostridium perfringens* (*Bacillus welchii*), *Cl. septicum*, *Cl. oedematines*, *Cl. sporogenes*, *Cl. histolyticum* and *Cl. fallax* (all of which yield exotoxins like *Cl. tetani*) has been prepared. Results obtained with a combined toxoid from *Cl. tetani*, *Cl. perfringens* and *Cl. oedematines* are believed to be promising. This product is not yet available commercially.

Passive immunization, as a preventive measure, with a combined antitoxin is highly recommended. The most practical product is the Tetanus-Gas Gangrene Antitoxin which protects against *Cl. tetani*, *Cl. perfringens* and *Cl. septicum*. 1,500 units* of antitetanus and 2,000 units* of anti-clostridia are given in a dose for prophylaxis. Larger doses are used in treatment of the disease. The use of anti *Cl. perfringens* serum has been recommended in abdominal surgery.

* These are U.S.A. Units. The International Units are half of the U.S.A. Units.

A Mirror of Hospital Practice

DIVERSE FINDINGS IN A CASE OF FATAL PERITONITIS

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WIDELY diverse laboratory findings, often incompatible and even antagonistic, in an otherwise well-defined clinical picture, not free from variations from day to day, confuse considerably.

A Hindu girl, the case under review, aged about 12 years, was admitted into the hospital on 14th October, 1947, with the following complaints of 8 days' duration:—

- (1) Continuous fever.
- (2) Headache and pain in the joints.
- (3) Slight unproductive cough.

The onset of the fever was attended with chill and was accompanied by pain all over the body and swelling of the left ankle, left knee, right knee, and right ankle in succession. Constipation was present.

On examination, the patient was quite conscious but irritable when disturbed. She was lying curled up in bed. The skin was flushed. The temperature was 102.4°F., pulse 112, respiration 32, blood pressure 97/70 mm. of Hg. There was no anaemia, cyanosis or jaundice. The tongue was coated at the centre and red at the margins, moist and slightly tremulous. Liver and spleen were not palpable. Pulmonary second sound was accentuated and there was a soft systolic murmur over the mitral area without any conduction. There was no discharge from the ear or tenderness over the mastoid process. Lungs were clear. The neck was rigid and painful but Kernig's sign was negative. The joints were swollen, hot and tender but there was no sign of fluid.

Blood count done on the day of admission showed W.B.C.—45,000 c.mm., poly—96 per cent, lympho—4 per cent, malaria parasites—not found.

The patient was put on sodii salicylas gr. 15 every 4 hours in view of the swelling of the joints, but penicillin was started, 20,000 units

intramuscularly every 3 hours, when the high leucocytosis was revealed. This brought down the temperature next morning to normal, but towards the afternoon it rose again to 103.4°F. Lumbar puncture was tried but resulted in failure as the patient was very much irritable. Widal reaction was positive, To 1/250 on the 3rd day in the hospital, i.e. 11th day of the disease. Though the joint conditions improved slightly, the temperature continued between 100 and 102°F. Lumbar puncture, later, showed turbid fluid under slight tension (90 drops per minute). Sulphadiazine was started 2 gm. *stat* and 1 gm. every 4 hours along with penicillin already being given.

Report on C.S.F.: Cell count—6,000 per c.mm., mostly polymorphs. Smear examination—pus cells plenty. Culture showed staphylococci, believed to be contaminated.

Biochemistry of C.S.F.: Sugar—10 mg. per 100 cc., chloride—650 mg. per 100 cc., protein—240 mg. per 100 cc.

On the 4th day after admission to hospital, i.e. 12th day of illness, another blood count was done, which showed W.B.C.—17,000 per c.mm., poly—72 per cent, lympho—28 per cent.

The patient was now more toxæmic. Neck was rigid and painful and Kernig's sign was slightly positive, temperature ranging from 102 to 103°F.

Another lumbar puncture was done on the 13th day of illness and turbid fluid under slight tension obtained. It was repeated on the 15th day of the disease with similar results, total cell count being 2,110 per c.mm., mostly polymorphonuclears. Smear showed Gram-positive capsulated diplococci and culture showed diplococci pneumoniae.

Penicillin 20,000 units was given intrathecally. Blood count was: W.B.C.—18,200 per c.mm., poly—79 per cent, lympho—21 per cent.

There was a definite remission. The temperature dropped gradually to 97°F., pulse and respiration 88 and 22 per minute respectively. Blood pressure—95 to 60 mm. of Hg. The patient was feeling better and there was general improvement all round. Another Widal reaction of the blood was done and was found to be positive up to 1/400 (To). This was on the 15th day of illness. Th, however, was negative.

The temperature continued at 97°F. till the evening of the following day, i.e. the 17th day of the disease, but the pulse showed distinct tendency to acceleration, and the patient became restless. The pulse was feeble and fast—138 per minute. The respiration was 38 per minute. There was involuntary passage of urine. The bowels did not move. The abdomen gradually became distended and rigid and the liver dullness was obliterated. There was no sign of free fluid in the abdomen, and no intestinal peristaltic sound was audible. Surgical opinion was sought for and it was diagnosed as intestinal perfora-

tion. Her general condition was too bad for any surgical interference. Resuscitation was tried with plasma and saline. Gas gangrene antitoxin serum was administered. These were all of no avail at all and the patient gradually sank and expired in the evening of the 18th day and just before death the temperature rose to 102°F. No permission for autopsy could be obtained.

Discussion

The clinical picture of an irregular continuous fever of about 8 days' duration, with painful swelling of the joints and its fleeting character in a young girl of 12, would naturally point to an attack of acute rheumatic infection at first sight.

The high leucocytosis with marked increase of polymorphonuclear leucocytes, the curled up attitude, irritability and neck rigidity, even in the absence of Kernig's sign, would however suggest meningitis. The joint manifestations would easily and appropriately be made to fit in with it.

A continued fever of possibly longer duration than what history gives is possible. She might have been ambulatory for some days before taking to bed and this might account for early positive Widal reaction. The toxæmic state, the meningeal manifestation and the increasing titre of To, go in favour of typhoid fever. The high leucocytosis, unusual with enteric fever, could be accounted for, if we presuppose latent coccal infection as a hidden complication.

The increased tension and turbidity of cerebrospinal fluid, marked reduction of its sugar content and a fall in chloride would support the diagnosis of meningitis. But the first pathological report, i.e. presence of staphylococci in the smear and cocci in culture, was rather confusing and the pathologist thought that it was due to contamination.

The second report on the culture from C.S.F. from a fresh lumbar puncture revealed the presence of capsulated diplococci pneumoniae. Again the prompt relief of symptoms, rapid fall of temperature and the condition of general well-being by intrathecal penicillin would further support pneumococcal meningitis as a therapeutic confirmation. On the other hand, the rapid rise of serum titre to higher dilution. (To 1/400) in Widal reaction could not admit the total elimination of bacillus typhosus from the picture.

The absence of 'H' agglutinins, with increasing titre of 'O', does not point towards anamnestic reaction either. Stool and urine cultures were serious omissions. Notwithstanding rising Widal results, the predominant and sustained picture was that of meningitis. The enteric picture, however, followed the footsteps of the progress of the disease relentlessly and subserviently along with meningitis, the major causative agent, of which it was a formidable

rival. Its active participation and implications cannot be minimized or ignored. It actually came to the forefront, pushing meningitis into the background when the intestinal perforation and peritonitis finished the picture and brought about the end. That the end resulted from perforation was also the opinion of the surgeon who thought that the condition was unsuitable for operative interference.

The pneumococcal infection, as evidenced from culture of C.S.F., could not be brushed aside and needs retrieval because the abdominal catastrophe could equally be ascribed to a fulminating pneumococcal peritonitis, the whole diseased process being a pneumococcal infection manifested earlier in meningitis and later in peritonitis. The case may further be considered to be one of double infection arising out of diplococcus pneumonia and Eberthella typhæ.

The rapid improvement of the general condition and general well-being obtained from the intrathecal administration of penicillin, as already pointed out, were of a transitory nature. In an otherwise disruptive and fulminating double infection, the combined lethal effect was exerted on the peritoneum resulting in an abdominal catastrophe which might have been equally produced from intestinal perforation due to typhoid infection, or from pneumococcal peritoneal infection, manifested earlier in meningitis, or from both.

Thanks are due to Dr. S. C. Sinha, Superintendent, Lake Medical College Hospital, for his kind permission to publish this report, and also to Dr. B. Biswas for his help in this investigation.

A CASE OF HEMIPLEGIA

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THE following case is presented on account of many unusual features.

The history briefly is as follows :—

Male, aged 40, admitted to the Irwin Hospital for complete hemiplegia of the left side, left hemianopsia and partial sensory loss of the left side. Babinski-extensor both sides. The patient had eight attacks of left hemiplegia in a period of ten years at varying intervals. Blood and C.S.F.—Kahn test negative.

The patient died after admission and a partial autopsy was done, only the brain being examined.

The brain.—The right hemisphere was slightly depressed when compared with the left. There was a thick gelatinous material on the right hemisphere which was brownish on the superior portion along the inner side. Basal blood vessels showed no abnormality except that there was a small whitish nodular area of atheroma on the basilar artery. There was no basal meningitis.

On cutting the brain by a sagittal section, the left side showed no abnormality. On right side an area about half an inch deep and extending practically throughout the length of the hemisphere on the medial side showed gelatinous-looking tumour-like tissue with areas of hæmorrhage.

Histological examination

1. Basilar artery—atheroma and post-mortem clots.

2. Sections from the gelatinous-looking mass which appeared like a tumour showed good deal of hæmorrhage, degeneration and thrombosis in the blood vessels.

3. In some sections were seen large blood vessels with thrombi which had undergone organization and canalization. There was a abundant collection of neuroglial cells in several areas.

From the histology it is clear that this particular person suffered from thrombosis of cerebral vessels on several occasions. The process of thrombosis being followed by recovery until the last attack which proved fatal.

The autopsy on a case of hemiplegia by itself can be said to be comparatively uncommon. Looking through the index of autopsies in the Pathology Department of the Grant Medical College, Bombay, there are 156 recorded autopsies of hemiplegia in a total of 10,000.

Therapeutic Notes

NOTES ON SOME REMEDIES

XXVIII.—DRUGS IN HELMINTHIC DISEASES, Part III

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*Treatment of helminthic diseases**

(1) *Ascariasis*

1. *Santonin*.—Preliminary fasting is not advisable since absorption of santonin is enhanced in an empty stomach. The patient takes an early light meal in the evening, and santonin 3 gr. mixed with an equal amount of calomel is given at bedtime, followed by a saline purgative the next morning. Repeated treatment may be necessary but at intervals of not less than a week.

2. *Hexylresorcinol*.—It is prescribed in the form of caprokol 'cristoids'. In the morning the patient takes 1 gm. of the drug, in five 0.2 gm. capsules, on an empty stomach, taking care not to chew them. Two hours later a saline purge is

* Diseases for which there is no effective drug have been omitted. Doses mentioned here are for adults only; for children see table in the previous article.

given to remove the worms, or it may be postponed till next day. No food is given for 4 hours after administration of the drug. The treatment may be repeated in three days.

3. *Oil of chenopodium and tetrachlorethylene*.—This combination is recommended when ascariasis complicates hookworm infection. After a saline purgative on the previous day the patient takes in the morning a mixture of tetrachlorethylene (2.7 cc.) and oil of chenopodium (0.3 cc.) in capsules or on sugar in a spoon, or the mixture can be shaken up in magnesium sulphate solution and taken. The mixture can be given to children in a dosage of 3 minims per year of age. A saline purge is given 2 hours later. The patient should remain in bed and not take any food till the bowels have moved well. The treatment may be repeated after 7 days. See also remarks under hookworm infection.

(2) *Oxyuriasis (threadworm infection)*

The adult worms inhabit the cæcum and the adjacent portions of the ileum and colon. The females migrate and deposit eggs in the peri-anal region, causing pruritus and probably nervous disturbances in young children. These eggs re-infect the host through fingers and expose other individuals to infection through contaminated bed clothing. Usually more than one individual in a family is infected.

1. *Gentian violet (medicinal)*.—Two 0.5 gr. 4-hour enteric-coated tablets are given thrice daily before meals for 8 days; this is repeated after a week's rest.

2. *Hexylresorcinol*.—This is less satisfactory. The capsules are given in the morning as for ascariasis. The same night, after a preliminary wash with warm water, an enema is given with 250 to 400 cc. of a 1 in 1,000 solution of the drug and retained for 15 to 30 minutes. Two or three courses are usually sufficient.

3. *Tetrachlorethylene*.—Sometimes quite satisfactory. Used as for hookworms (*vide infra*).

4. There are many household remedies, e.g. high enema of salt water (2 tablespoonfuls of salt to a pint of water) or of fresh infusion of quassia, one or two pints being used after first cleansing the bowel with warm water. These are at first given daily, later bi-weekly or weekly. They are, however, not satisfactory.

General measures.—Cutaneous lesions around the anus caused by scratching are treated by applying ammoniated mercury ointment. To complete the cure, personal hygiene is as important as medical therapy: cutting finger nails short, cleaning the anal region with soap and water, and periodical disinfection of clothing by boiling.

To test cure, several peri-anal swabs should be examined.

(3) *Trichuriasis* (whipworm infection)

Like threadworms, these worms live commonly in the caecum and are usually asymptomatic. Children tend to acquire a heavier infection which may manifest in the form of diarrhoea, anaemia and nervous symptoms.

Treatment is unsatisfactory. The common anthelmintics (e.g. santonin, hexylresorcinol) are moderately effective in heavy infection but unsatisfactory in light infections. Craig and Faust in 1945 recommend (1) a saline purgative followed by a high enema of tepid salt solution and (2) next morning a dose of tetrachlorethylene (2.7 cc.) and oil of chenopodium (0.3 cc.). A second treatment may be given after a week.

(4) *Ancylostomiasis* (hookworm disease)

The worms attach themselves to the mucosa of the jejunum and suck the blood from the capillaries of the villi, causing in course of time much loss of blood and microcytic hypochromic anaemia which is a characteristic of the disease.

1. *Tetrachlorethylene*.—It is the drug of choice. After a saline purgative on the day before, 3 cc. of the drug is given in the morning, either shaken up in a saturated solution of sodium sulphate or in gelatine capsules or on sugar in a spoon. In the latter cases a follow-up purgative is given after 2 hours. A light meal is allowed only after a copious bowel movement has been obtained. The eggs of the worms may be passed in the faeces for a week after effective treatment. If they persist beyond this period, the treatment should be repeated.

2. *Hexylresorcinol*.—It is less effective than tetrachlorethylene, but being almost non-toxic is suitable for debilitated patients in whom other drugs are contra-indicated. It is used as for ascaris. Patients often continue to pass worms for 10 to 15 days after a single dose, so treatment should be repeated after a fortnight, if necessary.

3. *Carbon tetrachloride*.—A highly efficient drug, but it has some important contra-indications which have already been mentioned.

4. *Oil of chenopodium and tetrachlorethylene*.—This is given in a mixed infection of ascaris and hookworms. In such cases some prefer less potent drugs, using hexylresorcinol followed in a week by tetrachlorethylene.

5. For *mass therapy*, as in tea plantations, a simple mode of treatment is to give a mixture of tetrachlorethylene (2.7 cc.) and oil of chenopodium (0.3 cc.) in a solution of Epsom salts.

General measures.—It is most necessary to treat the anaemia by giving nutritious diet and iron medicinally. The latter is given as ferrous sulphate tablets or ferri et ammon citras in a mixture thrice daily for three weeks, and this is repeated after an interval. If macrocytic anaemia has developed, liver extract is indicated.

Anaemia, when severe, should invariably be treated first before putting the patient on anthelmintic therapy.

(5) *Strongyloidiasis*

These worms are said to be more common in the Punjab and Rajputana. They have a complicated life-cycle during which they may cause symptoms simulating broncho-pneumonia in the course of their migration through the lungs. Or the female worms upon reaching the intestinal tract may provoke mucous diarrhoea (which frequently alternates with constipation) from the irritation caused by their entry into the mucosa of the small intestine and deposition of eggs which hatch in the tissues. During the early stage of active infection there may be a high degree of eosinophilia (40 per cent or more).

Gentian violet is the best drug so far known. Two 0.5 gr. 1½-hour enteric-coated tablets are given thrice daily, one hour before meals, until 50 grains have been taken (i.e. 17 days). Two courses of treatment may be necessary. For refractory cases transduodenal intubation of 25 cc. of a 1 per cent aqueous solution of gentian violet may be effective.

A 4-day treatment has been developed by J. S. D'Antoni. Thus—

1st day—Two tablets (½ gr.) t.d.s. before meals.

2nd day—Three tablets (½ gr.) t.d.s. before meals.

3rd day—Four tablets (½ gr.) t.d.s. before meals.

4th day—Five tablets (½ gr.) t.d.s. before meals.

For pulmonary strongyloidiasis intravenous injections of gentian violet are recommended. The drug is used in a sterile 0.5 per cent solution, made up in distilled water and filtered. On alternate days 20 to 25 cc. of this solution are injected very slowly up to five doses. The patient should be under close medical supervision.

(6) *Teniasis* (tapeworm infection)

Infection occurs chiefly through eating beef or pork. The large tapeworms (*T. saginata* and *T. solium*) live with their heads embedded in the wall of the small-intestine and may give rise to no symptoms or cause mechanical obstruction by their mass or toxæmia due to metabolic wastes. The larvæ of *T. solium* (pork tapeworm) sometimes enter the blood stream, and becoming encysted in the tissues give rise to cysticercosis which may cause serious sequelæ when located in vital organs. Of the dwarf tapeworms, *H. nana* carries infection directly from man to man, which when heavy causes toxæmia with nervous manifestations in small children.

1. *Male fern*.—Partial starvation for two days is advisable before giving the treatment.

The patient is given 1 ounce of saturated solution of sodium sulphate on the previous evening and next morning on an empty stomach 60 minims of the oleoresin of aspidium or liquid extract of male fern are administered in three equal doses in gelatine capsules (*i.e.* 20 minims in each, at 7, 7-30 and 8 a.m.). At 10 a.m. another saline purge is given. He remains in bed and is allowed no food until a copious bowel movement has been obtained. All stools for 48 hours after treatment are saved and searched for the heads of the worms which are frequently discharged after the main portion of the worm has been evacuated. If not found, it is better to wait for a month or two till the segments reappear before repeating the treatment.

Another method is to give the following emulsion by duodenal intubation: Oleoresin of aspidium 1 drachm, saturated solution of sodium sulphate 1 ounce, mucilage of acacia 1 dram and water 2 ounces. No post-treatment purgative is necessary.

2. *Carbon tetrachloride* or *tetrachlorethylene*.—These are also effective. The former alone is the best if there is no contra-indication.

Associated anæmia is treated with iron or liver therapy.

(7) *Filariasis bancrofti*

Wuchereria bancrofti lives in the tissues, and may produce obstruction in the lymph vessels and swelling of the affected part. The worms eventually die and the resulting lymphangitis may end in elephantiasis. There may be no signs for a long time. The microfilaria (embryos) found in the peripheral blood do not cause any tissue reaction beyond periodical pyrexia.

There is no specific. The antimony salts reduce the number of microfilariae for varying periods, but the adult worms remain unaffected. Fouadin is given intramuscularly up to a total of 45 cc., the amounts on first three days being 1.5, 3.5 and 5 cc. and then 5 cc. on alternate days. Anthiomaline seems to give better results by reducing the microfilariae for a longer period, it may be several months. Two to 4 cc. of the solution are injected into muscle or vein on alternate days up to 10 doses. The treatment of elephantiasis is mainly surgical; scrotal cases give the most satisfactory results. Treatment of filariasis due to *Wuchereria malayi* is on the same lines.

A more promising drug is the new compound, hetrazan. It has possibly no direct lethal action on the microfilariae but it seems to modify them in some ways so that they are destroyed by the phagocytes of the reticulo-endothelial system. With 100 to 300 milligrammes daily by mouth in divided doses over a period of 3 to 7 days, the parasite quickly disappears from the blood stream, but reappears in a few days after the drug is discontinued. When it is given for 3 to

4 weeks, the parasite has in some patients remained absent for about a year. Reports suggest that hetrazan has only moderate effect on the adult worms, but prolonged intensive treatment may destroy them. Trials are not complete. It seems to be less effective on other filarial infections of man. Toxic symptoms so far observed are headache, lassitude and vague malaise. These symptoms come on within a few hours of the treatment being started, but usually disappear within 48 hours, even when administration is continued.

(8) *Schistosomiasis*

This has been dealt with in a previous article (*I.M.G.*, 82, 541).

General instructions on the use of intestinal anthelmintics

1. Most of these drugs are protoplasmic poisons and call for careful judgment before they are used in lung, liver and kidney disease, intestinal ulceration, fevers and marked debility.

2. Alcohol and fats favour their absorption in most cases, thus increasing their toxicity, so they should be withheld a day or two before and after treatment.

3. On the day previous to treatment the bowel is emptied of its contents as far as possible by a light diet and a purgative which may be a saturated solution of sodium or magnesium sulphate. Castor oil should not be used.

4. Next morning the anthelmintic is given on an empty stomach. Tea or coffee is allowed, but the usual breakfast is omitted.

5. A second purgative should follow two hours after the last dose of the anthelmintic to expel the dead or moribund worms as well as to remove the unabsorbed portion of the drug out of the intestine. Many clinicians find it convenient and effective to mix the purgative with the drug when prescribing carbon tetrachloride or tetrachlorethylene.

6. No food is allowed except water until a good post-treatment bowel movement has been obtained. First give fruit juices with ample sugar and later a light meal.

7. Except in the case of non-toxic drugs like hexylresorcinol the patient should be resting in bed during treatment.

8. Toxic symptoms are mainly of three types—gastro-intestinal irritation, inflammation of kidneys and nervous manifestations including disturbances of vision. There is no specific antidote and the usual treatment consists of purgative, enema, and stimulants to avert collapse, chloroform for convulsions, etc.

9. In most cases the treatment may be repeated after a week, but it should be noted that the ova or the dead worms may continue to be passed in the faeces for some days after the treatment.

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Indian Medical Gazette

APRIL

THE KING'S HEALTH

WITH a view to improving the blood-supply to the right foot, and to safeguard this for the future, the operation of lumbar sympathectomy on the right side was performed on Saturday, 19th March, 1949, morning. A bulletin issued from Buckingham Palace on Monday, 21st March, signed by six specialists, states:

'The King's recovery from his operation has been uneventful. Instrumental tests have confirmed the substantial improvement in the blood-flow to the right foot, which had already been observed clinically after the operation.'

[Abstracted from the *Lancet*, 19th March, 1949, p. 488 and *B.M.J.*, 26th March, 1949, p. 544.]

PNEUMONIC PLAGUE IN EASTERN INDIA

NEWS came through in March that a party of pilgrims to Gaya from the Punjab had been nearly wiped out. Confirmation was sought and obtained. Eight persons had left for Gaya from the village Sail, P. S. and P. O. Sadarmandi (Kangra). One had sickened and died in the train. Six had sickened and died at Gaya. A homœopathic practitioner had been called to see the sick at Gaya. He too had sickened and died. Ten other members of his family had died in quick succession.

Positive laboratory findings were not available. Obviously 18 physically fit subjects after contact with one another had sickened and died rapidly, presumably from pneumonic plague, originating in the Kangra hills in the Punjab.

While waiting for further details from Patna, news, facts and proof followed one another rapidly concerning similar events quite close to and in Calcutta.

Vishnupada Charit, aged 20, grandson of Sannyasi Charit, a *modak** by profession, went to Bankul (a village on the Howrah-Amta railway and about 14 miles from Calcutta) to bring his grandmother for a bathe in the Ganges (Hooghli) on the occasion of *Baroni*. He was accompanied by his uncle, Kanai. He fell ill at Bankul and remained there. The old lady

and the uncle of the young man came to Calcutta on 26th March, 1949.

On the same day another uncle of the young man, Balai, went to the village and found his nephew very ill. The nephew had sickened from pneumonic plague and was the first case of a long series. The local physicians, however, had diagnosed the disease as malignant malaria but had failed to give any relief. Balai returned to Calcutta on 28th March, 1949, to get help.

Two other uncles of the young man went to Bankul with the old lady. That night Vishnu died. Present in the house then were the old lady, 2 uncles from Calcutta, other members of the family, residents of the village, and a near relation, all totalling 23.

Out of this number, 9 came to Calcutta and 14 stayed in the village. Of the former, 6 sickened. Five were admitted to a hospital and 1 remained at home. Out of those admitted to the hospital, 4 died and 1 recovered. The survivor had been given streptomycin. One who had remained at home also died. Out of the 14 who had stayed behind in the village, 7 sickened and died.

From the family of Sannyasi and his near relatives and friends, totalling 31, 13 people have died of pneumonic plague. The proof has been obtained and provided by Dr. S. C. Seal of the Epidemiological Department of the All-India Institute of Hygiene and Public Health. A detailed account by him appears in this issue elsewhere.

Last year in April we gave the readers an account of the first occurrence of plague in Calcutta in 1896 and its recurrence in our delayed March 1948 issue (*I.M.G.*, 83, March, p. 137). The last case of plague (death) was reported on 19th July, 1948. Since then all remained well in spite of rumours and even reports which we found baseless and ignored. The occurrences now described are different and call for action. The aforesaid Epidemiological Department having been forewarned last year is forearmed this year. With public co-operation all will be well again. This is no occasion for panic, inaction or secrecy.

The present pleasant weather in Calcutta, as the following comments from the daily press show, is unfortunately not unfavourable to the incidence of plague.

'Calcutta is enjoying one of the coolest Aprils for many years. Records for the past 50 years indicate that only 1946 can show comparable figures.

The average maximum temperature for April has been 91.9°F. against a normal mean maximum of 96.80°F. The figures for 1945, 1947 and 1948 were 94, 99.3 and 95.2. In 1946 the figure was the same as this year.

The coolness is accounted for by the frequency of nor'westers. There have already been 11 this

* A *modak* is a dealer in sweets made from rice. He keeps stocks which are likely to supply food for rats. The aforesaid *modak* has 3 shops: 2 *modak* shops proper and 1 grocery store.

Mukden in 1946, sulfadiazine was administered to four plague contacts who were proved carriers of *P. pestis* with the subsequent disappearance of the carrier state (Tieh *et al.*, 1948). Also Huang *et al.* apparently prevented secondary cases among the 60 odd contacts of a primary pneumonic plague patient by the administration of 3 to 6 grammes of sulfadiazine daily for one week (Huang *et al.*, 1948). Until more is known concerning the rate of infectivity of pneumonic plague patients (Wynne-Griffith, 1948), it is impossible to evaluate the efficacy of these drugs as prophylactic agents in plague. The recommendations of the Study Group of OIHP/WHO in this regard (Office International d'Hygiene Publique and World Health Organization, 1948) deserve careful application in a field trial when the occasion arises. Similarly, streptomycin is available as a prophylactic; there is, however, no published record that it has been used for this purpose and it is doubtful if this antibiotic recommends itself for large-scale use as a prophylactic, largely because of the need for parenteral administration.

The value of active immunization by means of vaccine deserves further consideration under carefully controlled and accurately observed conditions. Continuing studies on plague at the University of California have added much to the knowledge concerning the immunizing activity of the various antigens of *P. pestis*. It seems fairly certain from some of these reports that both living and dead plague vaccine may be effective if sufficient amounts of the two major antigens are present in the vaccines. However, before this type of prophylaxis will gain widespread popularity, some method must be devised to prolong the protection thus stimulated; at present, repeated inoculation of large doses of vaccine and the need for frequent recall doses is required to maintain a high degree of protection. Simeons and Chhatre (1947) confirmed this pessimistic outlook for vaccine by observing in a field study that resistance seemed to reach its maximum within 4 months of the injection; and their criterion of maximum resistance was based on the likelihood of recovery rather than prevention of the disease. Patel and Rebello (1948) made a similar observation that a single dose of vaccine reduced the case mortality rate by about 20 per cent and the morbidity rate by a narrower margin over those people not previously inoculated.* While the immunity conferred by a potent vaccine is of uncertain duration, there seems to be little doubt that the mortality is less among vaccinated populations than among those who have not received any inoculations of

vaccine (Chinese Ministry of Health, 1945). Yet, it does not require clairvoyance to predict that plague vaccines will lose their popularity as more potent antibiotics which are inexpensive and easy to administer are developed for the treatment and control of bacterial infections.

While serum has been available as a therapeutic agent in plague for many years, its use has never been popular. These sera have usually been of low antibody titre and their efficacy remains unproved. Macchiavello recommends further trial of serum only when other anti-plague chemicals and antibiotics are not available and feels that its use is without effect after the fifth day of illness. A potent anti-plague serum was developed in the United States during the recent war but its clinical value awaits field trial.

Reports continue to accumulate to confirm the efficacy of certain sulfonamides as anti-plague therapeutic agents. In a well-controlled series observed by Sokhey and Wagle (1948) it was demonstrated conclusively that both sulfadiazine and sulfamerazine significantly reduced the case mortality rate in both septicæmic and non-septicæmic plague. At present, sulfadiazine or one of its methyl derivatives is the drug of choice (Gordon and Knies, 1947; Chinese Ministry of Health, 1945; Sokhey and Wagle, 1948; Datt Gupta, 1948). The report of 3 cures among 5 patients with pneumonic plague during the Mukden outbreak (Tieh *et al.*, 1948) is additional evidence of the efficacy of sulfadiazine because this form of plague has always been associated with great mortality. Sulfathiazole has also been found to be effective in treating plague; Shamanna and Hedge (1946), thus, reported survival of twenty of twenty-six bubonic plague patients after sulfathiazole therapy administered to native patients in their homes.

Meyer and his co-workers (1948) have paved the way for the more precise evaluation of anti-plague drugs by standardizing a method of reproducing plague pneumonia in mice. Subsequently, this group of researchers (Quan *et al.*, 1947) demonstrated the efficacy of streptomycin in plague infections of small animals, thus confirming the earlier observations of Wayson and McMahon (1946). Similar results were reported in laboratory studies from England during the past year (Herbert, 1947). Almost simultaneously, Huang *et al.* (1948) submitted for publication the report in detail of a human case of pneumonic plague successfully treated with a combination of sulfadiazine and streptomycin. That this cure was not fortuitous seems to be confirmed by the report of Videla (1947) in which 7 patients with bubonic plague recovered after treatment with streptomycin, anti-plague serum and sulfamerazine; four of these patients were bacteraemic and one of these four had meningitis. Similarly, a published report from India (Karamchandani and Sundar

* Note.—Patel and Rebello's interpretation of their own figures needs a critical analysis which we will undertake in a subsequent communication. Their figures actually show that attack rate is reduced to 1/3 and death-rate to 1/6 by single dose inoculation of Haffkine Plague Vaccine (formalin killed). This is high protection, but if the vaccine is used in two doses with booster doses very much higher protection can be expected.—EDITOR.

Rao, 1948) of the cure of five cases of bubonic plague is additional evidence of the value of this antibiotic; improvement was noted within 36 hours and the authors felt that most of these patients were moribund when treatment was instituted. Haddad and Valero (1948) report the prompt recovery of 3 patients with bubonic plague after streptomycin treatment who had not responded favourably to sulfonamide therapy. Meyer and Quan recommend doses of 0.25 gramme q. 4. h. in bubonic plague; but in septicemic and pulmonic plague, they feel that doses of 0.5 to 1.0 gramme should be administered every four hours.

Conclusions

Thus it appears that medical ways and means are available for a campaign to eliminate plague as a recurring threat to large segments of the world's human population. Ideally, the problem should be attacked by employing social, economic and engineering techniques as well as medical means. The elimination of the reservoir of the pathogen poses an almost insurmountable difficulty; at present, the judicious use of rodenticides in communities where plague of wild rodents is endemic seems a more expedient approach to this phase of the problem. The intermediate vector, the flea, constitutes the most vulnerable link in the chain of transmission and can be combated by the use of DDT in one of its several forms. Vaccines and anti-plague sera have been shown to be useful in preventing plague among contacts and susceptibles; expense and method of administration are factors which militate against their adoption as mass prophylactics. The recently developed sulfonamides and certain of the newer antibiotics are potent bactericidal and bacteriostatic agents but their usefulness as plague preventives awaits demonstration in field trials on a large scale. The usefulness of sulfadiazine in preventing secondary cases in small outbreaks of pneumonic plague has apparently been demonstrated (Tieh *et al.*, 1948; Huang *et al.*, 1948); until more is known concerning the infectivity rate of the average pneumonic plague patient, or until alternate contacts only are given the drug prophylactically, the protective advantage of the sulfonamides cannot be discussed with certainty. From our present knowledge of the activity of sulfonamides *in vitro* and the limited clinical application of the drugs in this respect, this group of chemicals seems like an ideal prophylactic; they are not only potent against most strains of *P. pestis*, but they are relatively inexpensive and have the further advantage that they are easily administered by mouth. The recommendation of the OIHP/WHO/Study Group (Office International d'Hygiene Publique and World Health Organization, 1948) concerning the prophylactic use of sulfonamides in pulmonary plague deserves prompt clinical application. It is not improbable that the administration of these drugs may shorten or eliminate the need for quarantine among this

group of potential patients. Sulfadiazine and its derivatives have been of proven value in treating plague and have the advantage of oral administration. The new antibiotic, streptomycin, has been shown to be an effective agent against *P. pestis* both in the test-tube and in the clinic; at present it appears to be the most reliable therapeutic agent in plague but has the one disadvantage that it must be administered parenterally and at frequent intervals. The potential rôle of the newer antibiotics, aerosporin, aureomycin and chloromycetin, in the treatment and prevention of plague awaits future trials.

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PNEUMONIC PLAGUE CASES IN CALCUTTA AND GAYA

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PLAGUE re-appeared in Calcutta in April 1948 after a lapse of about 25 years. An interim note on this outbreak up to 10th May, 1948, was published last year (Lal and Seal, 1948). Altogether 276 cases were reported; of these 173 were clinically diagnosed as plague and at least 35 cases were confirmed bacteriologically. Twenty-three cases died giving a fatality rate of 13.3 per cent. The remaining 103 cases were not considered as plague. Human cases were removed from practically all the wards of the city except wards 1, 16 and 21 and also from the suburban areas in Howrah, Hooghly and 24-Parganas. The peak of the outbreak was in the last week of April, which tailed off by the middle of May. The peculiarity of this outbreak was that the cases were generally mild except at the onset when 8 out of 11 cases died. A few turned out to be septicæmic, the rest being of bubonic type. In most instances, the organisms were scanty. Even the rats did not exhibit enormous number of organisms which one usually associates with spleen smears. This peculiarity has been observed during the present phase of plague in other places also, like Lucknow. Thus the mildness of disease was interspread with a few severe cases, a common feature also noted in the early phases of the last pandemic, and the origin of cases, their distribution and seasonal incidence were very similar. In the later phases of the last Calcutta and Bengal epidemic pneumonic cases were also reported but the instances were few and far between, as will be seen from the following records collected by Wu Lien-Teh (1926) :—

Pneumonic plague cases in Calcutta (1898-1907)

Year	Pneumonic cases	Percentage of total cases	REMARKS
1898	9*	4.7	11* other cases occurred at Backerganj among contacts.
1899	116†	13.4	Proportion too high.
1903	235	3.01	
1904	101	2.1	
1905	?	3.7-7.5	In District I only.
1906	190	6.5	
1907	219	5.5	

* The cases were all connected with one house.

† 7 cases occurred in connection with one house at Kalighat.

During this pandemic, besides the instances stated above, small outbreaks of pneumonic plague cases were occasionally reported from other areas in India, viz, Bombay, Baroda, Cutch, Karachi, Kankhal, Jaswalpur, Madras, Punjab, N.-W.F.P. and Kashmir. Barring a few exceptions the pneumonic type caused little havoc in India in the last pandemic. In the summary of the work by the Indian Plague Commission (1908), it was considered that pneumonic plague was rare (less than 3 per cent of all cases) and that it played very small part in the spread of the disease. In the evolution of a plague epidemic, therefore, the character of the parasite particularly with reference to its occasional changes into virulent and pneumonic form is of great importance. The mechanism of this sudden change has still remained a mystery.

During this year plague cases began to appear a little earlier than last year, involving newer areas. One of these areas was the Orphanganj-Kalibazar market at Kidderpore, from which the

Pneumonic plague cases in Eastern Bengal

Year	Month	Locality	Cases	Deaths	REMARKS
1898	September	Backerganj	11	11	Introduced from Calcutta.
1899	(i) Feb.-March	Pania village	42	38	Do.
	(ii) March	Faridpur	30	29	2 bubonic cases preceded the pneumonic cases.
1906	(i) March-April	Serajganj	27	24	Introduced from Calcutta.
	(ii) June	Mymensingh	5	5	Do.
	(iii) August		50	45	Do.
1907	January	Malda	4	4	Introduced from Balia.
1910	June	Noakhali	51	45	Introduced from Calcutta.
1911	?	Faridpur	17	17	Do.
TOTAL ..			237	218	

The records of pneumonic plague cases, all fatal, in Calcutta; as collected by Crake (1908), are given below. Except in two instances the authenticity was not, however, mentioned.

first case of pneumonic plague, reported here, was introduced into a village called Bankul, about 14 miles away from Howrah. Altogether 130 cases have been reported till the 25th April,

1949. Of these 14 are now considered to be of pneumonic type occurring among the contacts of the case mentioned above. The history of this incident is described below :

History of the Calcutta outbreak

The sons of Sannyasi Charit (Modak), aged 82 years, namely, Kishori, Hrishikesh, Kanai* and Balai, belonging to the village Bankul in the District of Howrah, were running 3 shops*—2 at Kalibazar (1 grocer and 1 modak contiguous to each other), and 1 at Orphanganj market, in Kidderpore (Calcutta). They had also engaged several shop assistants for running their business. Kishorimohan lives with his family in a room on the first floor of 96, Diamond Harbour Road. The other brothers with their nephew Bishnupada, the shop assistants and one co-villager, Tinkori Bhattacharya, were staying in one room tenement on the first floor of Kalibazar at 106, Diamond Harbour Road, Kidderpore. Another room of the same building was occupied by Haricharan, son-in-law of Sannyasi. They had their families at Bankul, which they used to visit weekly and by turn; their old parents—Sannyasi Charit and Nagendrabala—were also living in that village home.

On the 25th March, 1949, Bishnupada, aged 20 years, along with his uncle Kanai, went home (Bankul) and was attacked with fever late that evening. Next morning, Kanai came back to Kidderpore with his mother who wished to have a bath in the Ganges on the occasion of the 'Baruni' festival. The same day (26th March), Balai, another uncle, went from Kidderpore to Bankul and nursed Bishnupada for 2 days. The local doctors were treating him as a case of malignant malaria with no effect. Balai, therefore, returned to Kidderpore on 28th March to obtain help. So Kishori and Hrishikesh rushed to Bankul with their mother. The former returned to Kidderpore in the evening and went back to the village next morning with ice only to find, to his misfortune, that Bishnupada had died the previous night (28th March). He returned to Kidderpore the same day (29th March).

Shanti, aged 4, daughter of Hrishikesh, took ill on Tuesday night (29th March) with similar symptoms and died on 31st March, in spite of treatment by the local doctors as a case of malignant malaria. Kanai returned to Bankul from Kidderpore in the evening of 29th March and remained there since then. While Shanti fell ill at Bankul, Balai was attacked with fever at Kidderpore on the same day. The local doctors treated him as a pneumonia case with penicillin, etc., but he expired at 11-30 p.m. on 2nd April in the

residence of Kishori at 96, Diamond Harbour Road. In the meantime, Tustapada, son of Kishori, who was at Bankul fell ill with the same symptoms on 31st March and was removed to Kidderpore the next day. One of the local doctors (Dr. Ajit Mukherjee) who had treated Balai, finding the same symptoms appearing in Tustapada, referred the case to the Medical College Hospitals on 2nd April (midnight) for diagnosis and treatment. It is said that he was given some sulphadiazine, as penicillin had no effect in the other case. This was the first case in the chain to be admitted into a hospital. Unfortunately, this boy died a few hours later on 3rd April, before a complete investigation was carried out. He had rigidity of neck muscles and positive Kernig; a lumbar puncture was done with negative results.

Three other cases occurred before Tusta got ill. One, Purnachandra Ghosh, the compounder of a local doctor who attended Bishnupada the first case during the whole of Sunday (27th March), got fever on the night of 30th March at his father-in-law's place at Baharya where he had gone for a visit, and died on 4th April. Nandarani, the mother of Bishnupada, who attended the latter all throughout, was attacked on 30th March and died within 48 hours on 1st April without any treatment. She developed a few hemorrhagic spots on her body and this led to a suspicion that the cases at Bankul were of suppressed smallpox, and accordingly the inmates were vaccinated against smallpox by the health staff on 5th April. Pannabala, widowed daughter of Sannyasi Charit, fell ill on 31st March and died on 3rd April. This was the first case at Bankul in which the probability of plague infection of pulmonary type was thought of by a local doctor (Dr. A. Dutt) and thus the inmates and some neighbours were vaccinated against plague by the health staff on 7th March, 1949.

The other victims at Bankul who followed suit were Sannyasi Charit and Nagendrabala, the grand-parents of Bishnupada, and Radharani, a woman from the neighbouring house, who came to nurse Panna and Nandarani, the dates of onset of their illness being 1st, 6th and 1st April, 1949, and of their death 3rd, 9th and 3rd April, 1949, respectively; thus the last case in the series to occur at Bankul was Nagendrabala, who fell ill on 6th April, 1949.

While this tragedy was being enacted at Bankul before the final curtain fell there, another series of misfortunes which was going on at Kidderpore (Calcutta) in the meantime may now be narrated. Hrishikesh, having lost his child, Shanti, and himself feeling unwell, thought that he could probably save himself and his family by leaving Bankul immediately, and so he left with his family consisting of the remaining five

* Selling sweets, puffed and fried rice and groceries. Obviously the stock of groceries, rice and paddy attracted a lot of rats.

members for Kidderpore on 1st April to stay at 106, Diamond Harbour Road. The same evening he was attacked with fever followed by symptoms of lung involvement as in other cases. On 3rd April, he was removed to Medical College Hospital, where he died the next day (4th April), practically undiagnosed. He was followed by his son Ratan and wife Champabala, both of whom were removed to the same hospital on 6th April, where Ratan died on 11th April but Champabala gradually recovered; treatment with streptomycin was started on suspicion from 7th April. All of them were sent to hospital by the same doctor who sent Tustapada, the first hospital admission.

Ratan was the first case whose blood was collected for culture and found on 11th April, 1949, by Dr. S. C. Ghosal, Professor of Bacteriology, School of Tropical Medicine, to yield *P. pestis*, later confirmed by mouse inoculation test and serology, the mono-specific serum being supplied by the author.

The last case to be admitted into this hospital was Haricharan Rana, son-in-law of Sannyasi Charit, who attended funerals of Panna and Sannyasi at Bankul and cases in Hrishikesh's family at Kidderpore. On 6th April, 1949, he went to Bankul for the last time. He fell ill on 7th April and the same day went to Khantora, his native village near Domjur on the Howrah-Amta Railway. He was removed straight from there to the Medical College Hospital on 9th April, where he developed the pulmonary symptoms like other cases and died on 12th April, 1949. *P. pestis* was isolated by Dr. Ghosal both from his blood and lung puncture material. Blood culture of Champabala taken after some doses of streptomycin proved negative but she was perhaps the only case in which sputum was found coloured and blood-stained. These cases were admitted into the wards of Drs. Das, Nandy and Sinha respectively.

The chronological order of cases with main signs and symptoms which could be elicited through investigation has been given in figure 1 and chart I and the familial and extra-familial relations of the cases in chart II.

The common symptoms from which all cases had suffered were :

- (1) Fever starting low and gradually rising high and going down again towards the end.
- (2) Easy mild cough without noticeable expectoration and pain in the chest and abdomen.
- (3) Respiratory difficulties beginning from the 2nd day, hurried respiration (rates varied between 30 and 60 per minute), dyspnoea and catarrhal signs all over the lung (œdema lungs ?) towards the end; other signs of lung involvement were also detected in many of the cases.
- (4) Signs of toxæmia and restlessness, and in a few cases congestion of the eyes; soft, rapid pulse becoming imperceptible towards the end.

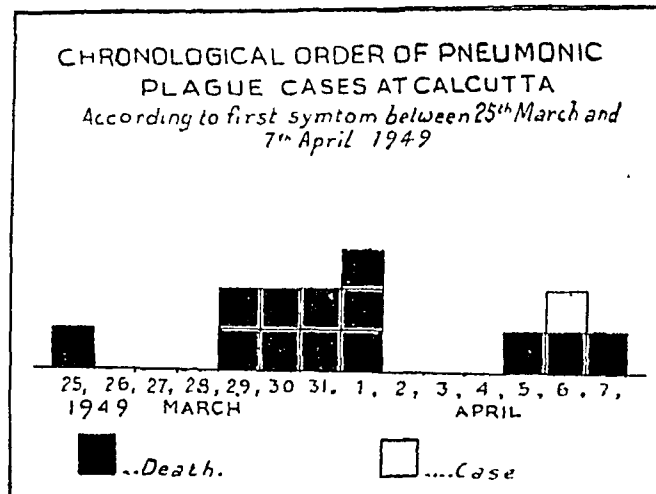
(5) Mental symptoms like delirium and incoherence (mania in some cases), but consciousness was not lost in most of the cases till the end.

(6) Diarrhœic stools.

(7) Appearing seriously ill without sufficient local signs to account for it. Deaths were generally sudden probably from heart failure.

Other signs and symptoms.—Patients 3 and 7 (both children) showed rigidity of neck muscles, tremors and twitchings; no. 3 also had

Fig. 1.



convulsion and no. 7 Kernig positive. Nausea and vomiting were present in a few cases. Spleen was found enlarged in some. Jaundice was noticed in patient 14; hæmorrhagic spots were seen on the chest and armpits of patient 5 and some diffuse subcutaneous hæmorrhage in the left forearm of patient 12. Sputum of patient 13 was found coloured and blood-stained. No glandular swelling was reported by any of the attending physicians except in patient 14 in which neck glands were palpable.

There were altogether 14 cases with 13 deaths. All the eight cases which occurred in the village (including one at Baharya) died, while 5 died out of 6 cases at Calcutta. From charts I and II it will be seen that the cases occurred only among the very close contacts and family relations. Cases 2 to 8 were very close contacts of case 1, cases 6 to 8 being also contacts of case 3; the rest of the cases were contacts of the patients 3, 6 or 9, while cases 11 and 13 at Kidderpore were contacts of case 8. Similarly, the two extra-familial cases, the compounder and a neighbouring woman, were both engaged in nursing the patients. According to this contact history the incubation period was short, generally about 2 days, particularly considering the time of death of the patients. All cases except one who is alive became rapidly fatal, the death occurring generally between 2 and 3 days. In two cases death occurred within 5 days. Four cases received no medical treatment at all. None of

CHART I

Chronological order of pneumonic plague cases (with main symptoms)

Number	Name, age and sex	Direct contact of case number	Date and place of attack	Date and place of death	Main signs and symptoms	REMARKS
1	Bishnupada Charit, 20. M.	?	25-3-49, 9 p.m., Bankul.	28-3-49, 11 p.m., Bankul.	High fever, palpable spleen, congested eyes, restlessness, maniacal symptoms, delirium, toxæmia, soft easy cough without much expectoration, hurried respiration, dyspnoea, and diarrhœic stools. Treated as malignant malaria by local doctors. Death in 3 days.	Treated privately.
2	Balai Charit, 31. M.	1	29-3-49, 6 p.m., Kidderpore.	2-4-49, 11-30 p.m., Kidderpore.	High fever, pneumonic symptoms, toxæmia and diarrhœa —later œdema of lungs, air hunger, dyspnoea, no temperature towards the end. Treated as pneumonia with penicillin. Death in 4 days.	Do.
3	Shantibala Charit, 4. F.	1	29-3-49, 10 p.m., Bankul.	31-3-49, 10 p.m., Bankul.	High fever, with convulsion, rigidity of neck muscle, muscular tremor and twitchings, rapid pulse, hurried and difficult respiration, short cough, no spleen. Treated as malignant malaria by the local doctors. Death in 2 days.	Do.
4	Purna Ch. Ghosh, 30. M.	1	30-3-49, 8 p.m., Baharya.	4-4-49 (morning), Baharya.	Full history not yet available. Treated as malignant malaria. Death within 4 days.	Do
5	Nandarani Charit, 36. F.	1	30-3-49, 12 midnight, Bankul.	1-4-49, 8 p.m., Bankul.	High fever, toxæmia, restlessness, cough, pain in chest and abdomen, dyspnoea. Some bleb-like eruption on chest and armpits (? subcutaneous hæmorrhage), diarrhœic stools. Death in less than 2 days.	Untreated.
6	Pannabala Charit, 30. F.	1 and 3	31-3-49, 10 p.m., Bankul.	3-4-49, 8 p.m., Bankul.	High fever, restlessness, delirium, diarrhœa, cough, moist sounds in both lungs, no spleen, rapid and later imperceptible pulse, dyspnoea (possibility of plague infection considered). Death in 2½ days.	Treated privately.
7	Tustapada Charit, 18. M.	1 and 3	31-3-49, Bankul.	3-4-49, in Medical College Hospital, Calcutta.	High fever, toxæmia, semi-conscious, vomiting (once), spleen +, liver palpable, moist sounds in both lungs, neck rigid, Kernig +, abdomen tense; later patient became extremely dyspnoeic, hurried respiration, imperceptible pulse, and lungs full of catarrhal râles. Total leucocytes 18,000; polymorphs 80 per cent; was treated with sulphadiazine and quinine before removal to hospital. Death in 3 days.	Removed to Medical College Hospital, Calcutta, on 2-4-49, at 12 midnight.

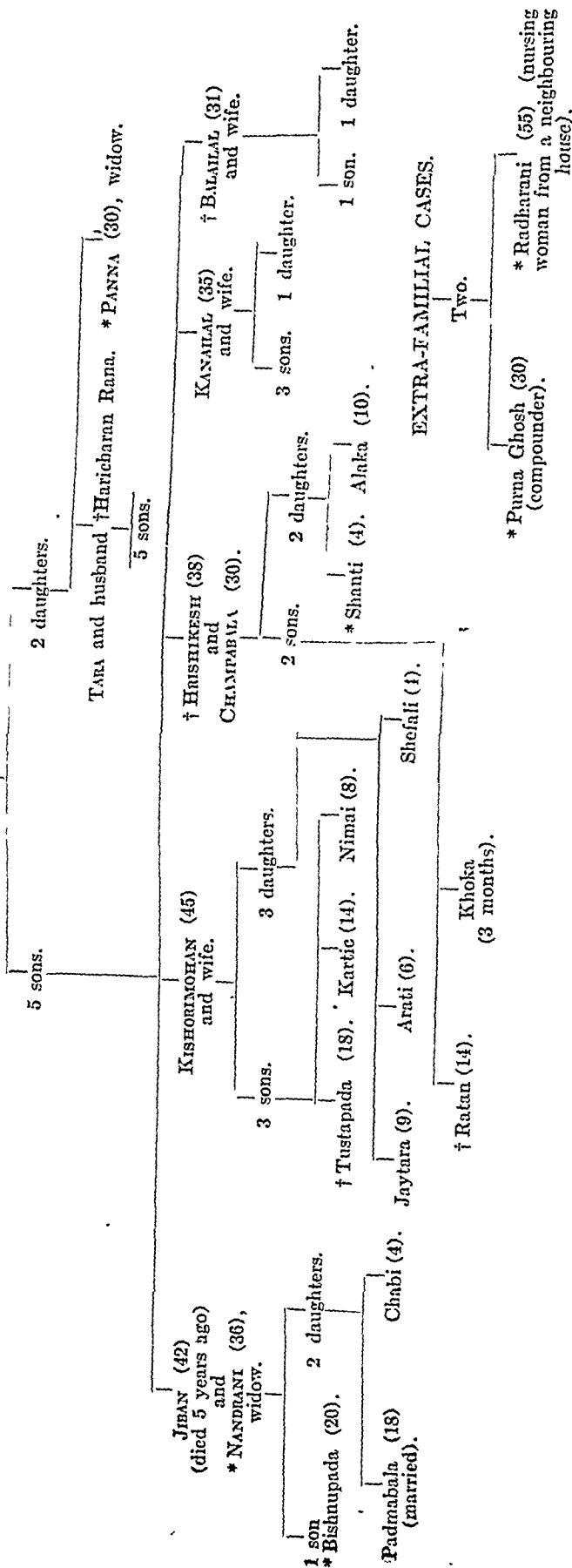
CHART I—concl'd.

Number	Name, age and sex	Direct contact of case number	Date and place of attack	Date and place of death	Main signs and symptoms	REMARKS
8	Hrishikesh Charit, 38, M.	1 and 3	1-4-49, Bankul, came to Kidderpore on 1-4-49.	4-4-49, in Medical College Hospital, Calcutta.	Continuous fever, toxæmic, restless, nausea and vomiting, spleen 1 finger, hurried respiration, passing stool and urine in linen; right middle lobe of lung—dull on percussion, breath sounds harsh with a few crepitations in the right, middle and lower zone (diagnosed as broncho-pneumonia), dyspnoic and delirium towards the end. Total leucocytes 9,050; polymorphs 80 per cent. Death in 3 days.	Removed to Medical College Hospital, Calcutta, on 3-4-49, at 11-45 a.m.
9	San'yasi Charit, 82, M.	3 and 6	1-4-49, 4 p.m., Bankul.	3-4-49, 10 a.m., Bankul.	Symptoms similar to patient 6. Death in 2½ days.	Untreated.
10	Radharani, 55, F.	5 and 6	1-4-49, 6 p.m., Bankul.	3-4-49, 10 p.m., Bankul.	Symptoms similar to patient 6. Death in 3 days.	Do.
11	Ratan Charit, 12, M.	8	5-4-49, Kidderpore.	11-4-49, in Medical College Hospital, Calcutta.	High fever, headache, pain in the chest, harsh breath sounds with a few rhonchi—both lungs. No spleen, very hurried respiration. Total leucocytes 10,800; polymorphs 72 per cent. Blood culture positive for <i>P. pestis</i> on 11-4-49. Death in 5 days.	Removed to Medical College Hospital, Calcutta, on 6-4-49, at 7-30 a.m.
12	Nagendrabala Charit, 65, F.	6 and 9	6-4-49, Bankul.	9-4-49, 12 a.m., Bankul.	Symptoms similar to patient 6. Death in 2½ days. Additional sign—subcutaneous oedema with hæmorrhage on the left forearm noticed after death.	Untreated.
13	Champabala Charit, 30, F.	8 and 11	6-4-49, Kidderpore.	Still alive	High fever, cough, pain in chest and limbs, worse on cough, headache, coloured blood-stained sputum. Streptomycin administered, patient still alive. Blood culture taken after streptomycin was negative.	Removed to Medical College Hospital, Calcutta, on 6-4-49, at 9 a.m.
14	Haricharan Rana, 34, M.	6 and 9 11 and 13	7-4-49, 6 p.m., Kidderpore. Left Khantora the same evening.	12-4-49, in Medical College Hospital, Calcutta.	High fever, pain in chest, dyspnoea, headache, occasional hiccough, semi-conscious, neck glands palpable, spleen +, jaundice +, eyes congested, hurried respiration, dullness over right infra-axillary region from 3rd space downwards to the base, diminished breath sounds and tubular breathing, increased V.R. and crepitations, later scattered moist râles all over, patient dyspnoic, death in 4½ days. Blood culture and lung puncture positive of <i>P. pestis</i> . Confirmed by animal and serological tests.	Removed to Medical College Hospital, Calcutta, on 9-4-49, at 2-40 p.m.

CHART II

Family relationship of the pneumonic plague cases

* SANYASI CHARIT (82) and
* NAGENDRABALA (65), wife.



* Died of pneumonic plague at Bankul.

† Died of pneumonic plague at Calcutta.

The figures in brackets indicate ages in years.

the cases or contacts excepting a few in the Medical College Hospital were inoculated against plague.

Strangely, many of the contacts who were close enough to the patients at one stage or the other escaped infection. For instance, of the 31 members of Sannyasi's family at Bankul and Kidderpore, only 12 showed symptoms and 11 died. No cases were reported among the contacts of the compounder who died at Baharya, nor amongst the six members of Haricharan's family at Khantora, with whom he came into contact, at least for a few hours. On investigation it however transpired that Haricharan intuitively apprehending the same fate as some of his relatives at Bankul warned the members of his family not to come too close to him. It is said that he went to his village home only to have a last look at his dear ones. Another close contact, Padmabala, sister of Bishnupada, who came from another village (Jhapardah) and nursed her mother (Nandarani) escaped. She was inoculated against plague on 7th April, 1949. Another visitor, a cousin of Kishori, who arrived there on the 3rd April and remained for 3 days also escaped. This can, however, be explained by the fact that no cases occurred in the family after his arrival except the old lady (Nagendrabala) who showed symptoms on 6th April, 1949, the day he left. All other attendants including doctors and nurses either at Calcutta or at Bankul also escaped. No cases were reported among the neighbours who attended the funerals nor amongst the distant contacts.

Comments

Bubonic cases of plague were reported from an area at Kidderpore about the same time when Bishnupada, normally residing there, moved out to Bankul and developed symptoms of plague with pulmonary involvement there. Rats in the locality, examined in the laboratory, were also found plague infected, while Bishnupada's shop was apparently rat infested. It is very likely that he originally received the infection through an infected flea and was in the incubation period during transit. It is difficult at this stage to say whether he actually developed any bubo, as no one looked for it in apprehension during his illness. The infection was probably severe enough to lead to septicæmia with lung involvement and this gave the bacteria the necessary momentum to be transmitted by droplet infection. The short incubation period in subsequent cases occurring only amongst close contacts in quick succession leaves no doubt that the transmission was by droplet infection. The possibility of an imported rat flea transmitting infection to so many patients was, if at all, extremely remote and *Pulex irritans* is not seen in this part of the country particularly among the local inhabitants. The incubation period is also against flea transmission. The

question of transmission factor, again, excludes the probability of all cases being purely septicæmic but it should be remembered that all pulmonary cases are *per se* septicæmic. *Pasteurella pestis* was isolated from at least two of the cases in the chain admitted into the Medical College Hospital. This finding when considered along with the characteristic signs and symptoms described above, the short incubation period and the most probable mode of transmission by droplet infection, leads one to conclude that the cases described here were of pneumonic plague.

Although the signs and symptoms observed here may not appear to many as typical of pneumonic plague it may be mentioned that cases with very little apparent lung involvement and expectoration have been described by various workers on pneumonic plague, particularly Wu Lien-Teh (1926) of Manchurian fame. According to the author the symptoms and signs noted in these cases when considered along with other findings were sufficient for diagnosing the cases as pneumonic plague, particularly in view of the fact that a disproportion between the general and local symptoms was noticed in all patients and that there was a deterioration of the general condition of the patient rather at an alarming rate. For a quick diagnosis, however, a portable x-ray equipment could be helpful.

Infectivity of pneumonic plague.—A question may now be raised why many of the contacts escaped infection. A general observation made in this series of cases, however, was that except in the case* who is still alive all patients had only soft non-productive cough. The chance of dissemination through droplets was therefore truly low. The only other way the author can explain the fact that no secondary cases occurred among the ward patients, doctors, nurses, and attendants in the Medical College Hospital† and other family contacts mentioned above is that a close and intimate contact whereby the persons breathe the exhaled air of the patient after a cough is necessary and that when a sufficient distance separates the patient from other persons the soft easy cough of the pneumonic plague patient was not sufficiently forceful in the present cases to propel the infection perhaps more than a few inches. The contacts in some cases were not probably prolonged enough to receive the infection. Besides, the patients are not generally infective at the early stages.

That cases of primary pneumonic plague do not invariably give rise to secondary cases even

* This patient who had shown some blood-stained sputum was fortunately partially segregated almost from the beginning.

† Only 14 out of 61 contacts were reported to have been previously inoculated against plague.

though there is a complete failure to quarantine or segregate contacts has been mentioned by the members of the International Plague Conference at Mukden in 1912 and by Strong (1942): and reported by Wu Lien-Teh (1926) in his treatise on pneumonic plague, and many others. Thus many close contacts in the Suffolk outbreaks escaped infection (Bulstrode, 1911). Wu Lien-Teh *et al.* (1923) record how on four occasions about 160 persons were exposed to infection by travelling in the crowded railway carriages with sick and dying patients with pneumonic plague without any of them contracting the disease. The latter authors (Wu Lien-Teh *et al.*, 1936) collected numerous other instances, from both literature and their own experience, of intimate contacts escaping infection. Among the recent records, Murdock (1940) described 3 outbreaks of pneumonic plague in Ecuador in 1939 in which the ward patients, nurses and doctors had escaped infection. Gale (1941) recounted an analogous instance. In another instance (Clark and Goldberg, 1943), 3 children slept in the same bed with a patient with pneumonic plague and yet escaped. Townsend (1944) stated that during an outbreak of pneumonic plague at Port Said 100 contacts were isolated, only 3 developed the disease. Munter (1945) reported a single case of proved pneumonic plague without a secondary case. Also Wynne-Griffith (1948) described an outbreak in Rangoon causing 16 deaths but showing low infectivity of the individual patients. In this outbreak, according to the author, the more or less intimate contacts of cases must have numbered over a hundred; seven doctors examined and attended several of these cases with impunity as cases of ordinary pneumonia and four nurses slept three nights in the same small room as their sick colleague but all of them escaped.

An incident analogous to that of Calcutta took place at Gaya (Bihar) only a few months ago, a short note on which is given below. It should, however, be understood that a complete investigation of this case has not been made.

Pneumonic plague at Gaya (Bihar)

Seven pilgrims came to Gaya town on or about 20th December, 1948, from Sail, a village in Sadarmandi (Kangra). Six of them died of pneumonic plague on successive days between the 23rd and 29th December, 1948. Another member of the party was also reported to have died on their way to Gaya. Most probably, the infection was originally contracted at Kangra (East Punjab). A local medical practitioner (Homoeopath) who attended on them at Gaya got infected and died. Following him 10 other members of his family of 18 contracted the disease and died in quick succession. The common symptoms observed in these cases were sudden high fever and headache with air hunger, breathlessness, extreme exhaustion and collapse. In most instances, mind was clear till towards

the end. On examination the patients showed catarrhal signs in the lungs but no definite consolidation.

The disease was practically confined to contacts of three houses and all the attacks excepting one ended fatally within two and a maximum of four days. The total number of deaths was 19. Some contacts escaped, although 4 or 5 of them had intimate contact with the patient during nursing. A provisional diagnosis of pneumonic plague was made but no further cases were reported since 3rd January, 1949.

Summary

Bubonic plague had been occurring in the Kidderpore area of Calcutta at the time when the present series of cases was reported. From this area a young man, apparently in the incubation stage, travelled up to his native village at Bankul, 14 miles away from Howrah, and there developed symptoms of septicæmic plague with pulmonary involvement. Thirteen other cases followed, all amongst close contacts—11 belonging to the family of 31 and 2 extra-familial. All except one out of 14 cases died. *Pasteurella pestis* was isolated from two cases in the chain admitted into the Medical College Hospitals, Calcutta. All cases more or less showed signs of lung involvement with soft cough mostly non-productive. The incubation period was short and fatality rapid. The most probable method of transmission was by droplets. The balance of evidence therefore was in favour of the diagnosis of pneumonic plague. Although most of the cases are now diagnosed retrospectively there is a strong presumption that the earlier cases were also of the same nature as the later proved cases of pneumonic plague. It is not, however, known whether this is the first time that such cases have been confirmed bacteriologically in the eastern part of India.

A large number of contacts including the attending doctors and nurses escaped infection. Similar experiences were previously described in the literature and one was recently narrated in an outbreak of pneumonic plague at Gaya in which the total number of deaths was 19 and a doctor's family, including the doctor himself, was the worst victim. As in Calcutta only one patient survived.

The following precautionary measures are suggested:

Doctors and health workers in an outbreak of plague, like the one now raging in Calcutta, should be on their guard and be suspicious of all patients with pneumonic symptoms and specially those who die in less than 4 days. They should also remember that the patients with pneumonic plague may cough very little and that the cough is soft and easy and the expectoration may be entirely absent in the early stages and very little or practically absent in the later stages.

No health worker or doctor should visit a suspected case of plague showing even slight evidence of lung involvement, without previously being inoculated and without a mask.

Immediate segregation of the patient by removing him to the hospital should be arranged and, if possible, at least one gramme of streptomycin be administered before hospitalization.

While the health organization should be informed to take other preventive measures such as preventive inoculation, disinfestation and deratization, etc., all the inmates of the house and probable contacts should be given 2 to 4 grammes of sulphadiazine daily for about 4 to 6 days and kept under strict quarantine and vigilance. Some antiseptic gargles and nasal douches may also be prescribed for them.

With these precautions it should be rather easier to control pneumonic plague than the bubonic in which large rat and flea populations are involved besides the human factor.

My best thanks are due to Dr. K. P. Bhattacharya, Plague Epidemic Control Officer, Government of West Bengal, for initiating the investigation of the Calcutta outbreak and for kindly offering his active assistance throughout. The co-operation and help received from the doctors, villagers, hospital authorities and health staff connected with this incident are thankfully acknowledged.

The information about the Gaya outbreak was collected through the courtesy of Colonel Duggal, the Director of Health Services, Bihar, to whom also my thanks are due.

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Postscript : I. Since this note was sent to the press, another case, Prafulla Kumar Das of Jorabagan area,

Calcutta, died of plague with lung involvement on 10th May, 1949. He started with a bubo and turned septicaemic (*P. pestis* was present in his blood smear and positive in culture), ultimately involving lung (his sputum showed *P. pestis*). He was removed to the hospital a few hours before death. Fortunately, no secondary case was reported (till 14th May, 1949). Sulphadiazine was administered personally by Dr. K. P. Bhattacharya, the Plague Epidemic Control Officer, to all contacts immediately after diagnosis. Two rats collected from the house also proved positive on 13th May, 1949.

II. 1949 outbreak (records made up to 7th May).

The cases began to appear towards the end of February, i.e. earlier according to the last year's record.

The total number of suspected cases up to 7th May, 1949 (reported in this delayed issue of April), including the 14 cases of pneumonic plague, are 189. Of these, 179 are considered to be clinically plague and 9 only non-plague. At least 47 cases have been proved bacteriologically positive including two of the pneumonic cases. The total number of deaths so far, including 13 of the pneumonic cases, is 34. Taking the mortality rate separately it was 12 per cent (21 deaths out of 175 cases) amongst the bubonic and about 93 per cent among the pneumonic.

Out of the places from which cases were reported special mention may be made of Howrah and 24 Parganas, the total number of cases so far being 42 and 13. The first case of plague to be bacteriologically diagnosed this year was from Ward 1 of Howrah where rat falls were previously reported and found positive. From the municipal area have been removed to hospital from as many as 25 out of the 32 wards. Besides above, 3 cases were removed from the Hooghly area, the new area involved being Baranagar and Alambazar, north of Cossipur area (Ward 32).

The total number of rats examined this year up to 7th May is 7,250 including 201 dead rats (i.e. 11,845 since the beginning of the outbreak). In 29 instances rats have been found infected.

The special feature of this year's outbreak is the occurrence of pneumonic cases and the continuance of the cases till now (23rd May, 1949). Probably the weather is chiefly responsible for it. The rat epizootic also seems to be extending.

The Indian Medical Gazette Fifty Years Ago

PROGRESS OF THE PLAGUE

(From the *Indian Medical Gazette*, Vol. **34**, 1899, p. 130)

THE onset of the hot weather has unfortunately not yet been attended by any considerable abatement of the epidemic as in the previous years. For the week ending the 11th March, 1899, the official summary shows that there was a continued increase of plague in Bombay City, the rise in reported plague-deaths being from 978 to 1,109 and in the total mortality from 2,309 to 2,444. There was a rise in the number of cases in Thana District, but no other important change occurred in the Bombay Presidency. Fifty-eight plague-deaths are reported from Karachi. There was a slight general improvement in the Madras Presidency. In Calcutta, there were 78 reported plague seizures with 66

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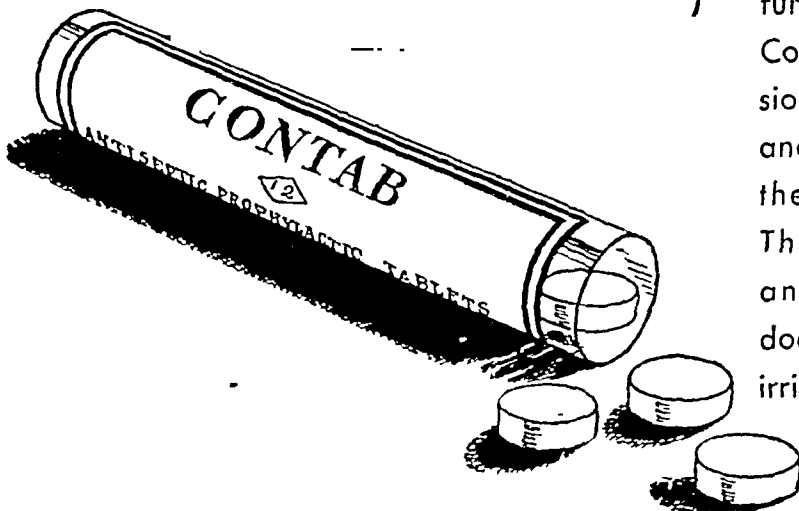
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deaths. Some isolated cases have been reported from Howrah and one from Serampore. Slight outbreaks have been reported from one village in each of the Dacca and Faridpur Districts. A considerable improvement has taken place in Mysore State, except that the number of seizures in Kolar gold-fields rose from 32 to 65. The figures show a great improvement in the Lingsugur District of the Hyderabad State. Plague had gained ground somewhat in the Jullunder District in the Punjab, there being 21 seizures during that week.

In Calcutta, the number of reported deaths from the pest has for some time averaged over twenty daily, inclusive of 'suspected' cases.

To check the spread of the disease from Calcutta to the interior of the province, more stringent inspection rules have been issued, with the following explanatory official note:—

'The reappearance of plague in Calcutta, and the occurrence of local outbreaks—all happily of small dimensions though of virulent character—in Bacergunge, Faridpur, Dacca, Saran and Darbhanga, in all of which it has been proved that the infection was carried by fugitives from Calcutta, have led the Lieutenant-Governor to the conclusion that steps must be taken to afford some protection to districts in the interior against the importation of infection from the town. Since December 1897, the only observation and detention camps have been those at Chausa, Mairwa, Chakradharpur and Khurda Road. These are all situated at or near the frontiers of the Province. Their object was to protect Bengal against the importation of the disease from other provinces to the west and south. From their situation they cannot and were not designed to act as a protection to Bengal districts against infection from Calcutta, and though for sometime past up-trains have been subject to inspection as well as down-trains, this measure was designed merely to prevent the carrying of infection outside Bengal. Now, however, Calcutta has itself become a centre of infection, and is by reason of its more constant intercourse with the mofussil, a more serious source of immediate danger than any infected area more remote. Steps must therefore be taken to guard the interior of the Province not only against infection from other provinces, but also from Calcutta. The measures which the Lieutenant-Governor thinks it necessary to adopt are set forth in Plague Regulation no. 15 of this date (29th March) which is published herewith. Nothing in the nature of land quarantine is proposed, or would be permissible. Nothing can or should, in the Lieutenant-Governor's opinion, be done to prevent persons not actually suffering from or infected with plague from leaving the town as freely as they please. Nothing is practicable which would seek to interfere with the enormous suburban traffic between Calcutta and its neighbourhood, or with the traffic that passes in and out of the town by

road or country boat. There seem, however, to be two measures which can properly be adopted, and which will afford to mofussil districts the protection they need, without hampering the legitimate movements of the people of Calcutta. The first of these is to ensure that no person who is actually suffering from or infected with plague shall be allowed when leaving Calcutta to travel by public modes of conveyance, such as rail or steamer. This is already prohibited by the ordinary law of the country; but the cases which have been mentioned above have shown that the prohibition needs to be enforced. The other is to arrange that when any person not suffering from plague leaves an infected area and proceeds to his home in the mofussil, timely intimation shall be furnished of his arrival to the local authorities in the district of destination. All such persons will be allowed to move about freely and without hindrance, but it is reasonable that the local authorities should have prompt notice of their arrival, in order that they may be forewarned and on their guard'.

The Royal Plague Commissioners left Bombay for London on the 25th March. Their report is expected to be issued in July.

Current Topics, Etc.

[Some of the topics under this heading are not exactly current. They have been held up because of special numbers for which they were not suitable. They are included because of their importance.—
EDITOR, I.M.G.]

Some Reflections on India

By J. L. COLLIS

(From *Queen's Medical Magazine*, Birmingham, Vol. 41, February, 1948, p. 24)

Misc was not a long stay in India. In all, I was sixteen months in the country, but it was an interesting time both medically and because great political changes were close at hand. I was a very interested and somewhat sympathetic observer, although I feel that it is most difficult for an Englishman to be really sympathetic in the circumstances. One was bound to identify oneself with the English ruler whose back they wished to see, while the daily newspapers contained such offensive remarks about our race, that one could not help but be irritated by them.

Nevertheless, it was true that all the anti-British feeling was against the system of government, and not against the individual Englishman. To myself, as an individual, all my many Indian friends were most kind, and I shall always treasure memories of their hospitality.

The educated Indians with whom I mixed are a highly intelligent set of people, so that it was easy to understand that the presence of foreign rulers with its inference that they were a backward race, was intolerable to their self-respect. They also felt that the government's interest ended provided law and order was maintained and vital services kept running. This, they regarded as being done in the interests more of British trade than for Indian welfare, which did not seem to them to be getting the really interested

attention that would be given by people of their own race. The unfortunate incidents which had occurred from time to time, were to the forefront of their minds, as being the reasons why they wanted to have their freedom, but I always felt that it was really the stigma of having foreign rulers that they resented more than the way in which their country had been ruled. In fact I felt quite certain that the country was not being ruled wholly badly. It was clear that many things should be improved, but the problems were of the most difficult nature, and of such enormous dimension.

The widespread poverty is the thing that impressed me most on arriving in India. I landed at Bombay which is a fine city, but even there the crowded quarters are unbelievably crowded by our standards. As I saw more of the country, the low productivity of the land, and the methods of agriculture, made the poverty of the dwelling places seem a natural result. The general effect is of miserable crops, and masses and masses of cattle hopelessly searching for a blade of grass. These are the problems underlying all India's difficulties, but what difficult problems to correct.

Irrigation schemes have done much, and can do much, and can do much more.

One basis of all society is that the average member of society must produce more than he needs for his own requirements. This surplus is then available for the individual's own amusements, and to supply taxes for such purposes as education, roads, hospitals and public services generally.

In India, the vast majority of the population appears to have no surplus at all, and in very many cases, it would seem they have a deficit. The result of this is that funds just are not available for the great changes that should take place. The only answer to this would seem to be that progress must be very slow. As religious change is also likely to be very slow, this would appear to make any faster progress quite impossible.

It must be remembered that progress has been going on under the British influence. Education has been pushed, but as funds were short, it has been limited to only a part of the population. This has been a good start, and these enlightened people now make the next step under Indian control possible. However, the farming population seems as yet to have been hardly touched and their problem must now be shouldered.

In India at present, there does seem to be a general awakening, which is running parallel with their demand for independence. The fruits of this awakening are not very evident as yet, but I feel certain that they will be seen in art, science, and industry, before long. Although I am confident that this is true, and although the Indian, as I have said, is an intelligent person, it is remarkable how sterile their minds have been in recent centuries. The British cannot be blamed for this situation. At least stable conditions have existed with the underlying revolutionary feelings which should have produced a fine mixture for original and creative thought and work. In any case, this sterility goes much further back than the British Raj. There were glorious days in the times of Elizabeth, when Akbar was ruling in Delhi, but the rule of the Grand Mogul, and especially the building of the Taj Mahal, appears to have been just a veneer on the surface of a mass of sterility.

Their real days seem to have been even earlier, in the time of Asoka 300 B.C., and perhaps the Imperial Guptas A.D. 300 which appear to have been the tail end of great times stretching back to the early Indian civilization.

These great changes of heart of a people seem to run in very long cycles, and are controlled by a multitude of factors, but it does seem that India is arising again. I see no short cuts for her, and I am afraid

some people in India will be disappointed when they come to realize this. Further, I do feel that the British have played their part in helping her back to her feet, and I would be the first to admit that this is only partly by the good we intended to do. The other part is by the stimulus that we have provided in their surge forwards for independence.

Chronic Hepatitis

By J. M. KILGOUR

(Abstracted from the *Canadian Medical Association Journal*, Vol. 58, May 1948, p. 437)

THE syndrome of chronic hepatitis is a distinct one which may follow either epidemic infectious hepatitis or homologous serum hepatitis. It is particularly liable to follow cases of the acute disease which have been allowed to return to activity before recovery is complete or in patients who have been undernourished, affected with concurrent disease or subjected to trauma or surgical operations at the time of onset but it does occur in the absence of any of these factors. The actual cause of the prolongation of the hepatitis is unknown. Complete recovery occurs in the great majority but a small percentage progress to cirrhosis. Four cases of thirty to forty months' duration have been presented, one of whom has proved cirrhosis, two presumptive cirrhosis and one with apparent complete recovery. It is possible that the progress may be arrested and complete functional recovery occur, even though cirrhosis has developed but as yet insufficient time has elapsed to exclude relapse in the cases reported. The most effective treatment at present is prolonged rest and maintenance of optimum nutrition until all clinical and laboratory evidence of activity has disappeared.

The Effect of Oral Administration of Casein Hydrolysate on the Total Circulating Plasma Proteins of Man

By F. CHOW

and

S. DEBIASE

(Abstracted from *The Journal Laboratory and Clinical Medicine*, Vol. 33, April 1948, p. 453)

CASEIN hydrolysate has been given to twenty-eight hypoproteinemic and hypoalbuminemic patients with a variety of diseases. It promotes the regeneration of both the plasma albumin and globulin fractions. In six cases of severe hypoalbuminemia, the albumin deficiency was corrected rapidly. Five hypoalbuminemic patients at the terminal stages of their diseases were able to utilize the hydrolysate to maintain a positive nitrogen balance but not to regenerate plasma proteins. These results are consistent with the belief that diverse medical and surgical conditions are characterized by varying degrees of protein depletion which can be corrected by large amounts of casein hydrolysate.

The Treatment of Lightning and Girdle Pains in Tabes Dorsalis with Niacin

By L. PELNER

(Abstracted from the *New York State Journal of Medicine*, Vol. 47, 1st July, 1947, p. 1496)

FEVER therapy and insulin shock treatment have also been used to allay the lightning pains. A degree of hypoglycemia which caused a slight somnolence and


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intense sweating in these treatments achieving an improvement in this in these treatments vasodilatation was also the common denominator.

Because of these theoretical points it was felt that niacin might be tried for this condition.

When it is injected intravenously in sufficient dosage, it uniformly produces a generalized vasodilatation. Subcutaneous injections and oral use of this drug are more haphazard in producing generalized dilatation.

The treatment used in this study was the intravenous injection of niacin as the monoethanolamine salt, 50 mg. per cc. Injections were started with 5 mg. and increased gradually twice weekly up to a maximum of 50 mg. (1 cc.). Within several minutes, a flush which lasted up to several hours was produced in each case. After several injections, the patient could dispense with analgesics. When the 50-mg. dosage was reached, it was given weekly for four weeks. After the injections were stopped, 100 mg. of niacin was given daily by mouth to prolong the effect.

Treatment of Hyperthyroidism

By G. CRILE

(Abstracted from the *Canadian Medical Association Journal*, Vol. 57, October 1947, p. 359)

TWO HUNDRED AND EIGHTEEN patients with hyperthyroidism have been treated with propyl-thiouracil in the past year.

There has been one death, and this was probably unrelated to the use of the drug. There has been one serious complication, exfoliative dermatitis, with recovery.

Minor side reactions including granulopenia, urticaria, arthralgia, nausea and sensations of 'numbness' have occurred in less than 3 per cent of the patients treated and have only twice necessitated interrupting treatment.

The dosage used, 200 to 300 mg. daily, appears to be on the minimal side of the effective dose and in some instances does not appear to be sufficient to effect and maintain a remission.

The drug has not as yet been withdrawn from a sufficient number of patients to allow estimation of the percentage of cases in which long-standing remissions will occur. Judging from the prompt remissions that have taken place in the patients who have of their own accord discontinued treatment after a few months of control, it does not appear that the incidence of remissions will be as high as had been hoped.

If the patient is co-operative and intelligent and can be observed by a physician who is familiar with the physiology of the thyroid and the pharmacology of the antithyroid drugs, treatment can be carried out safely and effectively over long periods of time.

When the patient is ignorant or unco-operative or cannot be observed periodically it is preferable to prepare the patient and perform a thyroidectomy.

Patients with small or moderate sized diffuse goitres with mild or moderate hyperthyroidism, patients with recurrent hyperthyroidism, and patients whose life expectancy is short, regardless of the type of goitre, may safely be given a trial on medical management for a year or more. If they respond favourably and prefer medical treatment this can be continued indefinitely. If they respond poorly or desire surgery a subtotal thyroidectomy should be performed.

Radioactive isotopes of iodine have been shown to be capable of controlling hyperthyroidism in most of the cases in which adequate doses have been given. Since the long-range safety of this form of treatment has not as yet been established it should be used with caution and in carefully selected cases.

Methyl thiouracil in doses of 200 to 400 mg. daily appears to be more effective than propylthiouracil in producing a prompt and complete remission and in a small group of cases has not proved toxic.

Penicillin and Sulphonamides in Typhoid Fever

(From the *Medical Journal of Australia*, 1st May, 1948, p. 559)

TYPHOID FEVER is sufficiently rare in this country nowadays to make the assessment of methods of treatment rather difficult. Occasional cases do, however, occur, and it is important to know the value of modern forms of therapy. In 1916 C. J. McSweeney reported the results of treatment with sulphathiazole and penicillin of six subjects of typhoid fever admitted to the Cork Street Fever Hospital in Dublin; the effects appeared to be rapid and satisfactory, although McSweeney readily admitted that it was unwise to draw general conclusions from such a small series of cases. It is interesting and necessary to note a report in the same issue of *The Lancet* in which R. Winston Evans described his investigation of the sensitivity of 66 strains representing 16 different phage types of *Bacterium typhosum*; he found a considerable variation of sensitivity which was independent of the phage type. Both of these reports are referred to in a recent discussion on the subject by C. G. Parsons, who summarizes the experience of physicians in military hospitals in the Middle East where cases of typhoid fever are constantly under observation. Results and opinions of the value of the treatment were collected from various hospitals, a control group being observed in each case. There was a total of over fifty cases. Parsons explains with complete frankness and in detail the anomalies and flaws in the data and declines to make any statistical analysis of the figures. However, he quotes the opinions of the physicians concerned at the various hospitals and, as independent observers, the unanimity of their impressions is rather convincing. In practically every case 'the natural history of the disease' (as one physician expressed it) 'was quite uninfluenced by the treatment with penicillin and the sulphonamide'. In a few isolated instances it was thought that the treatment caused some reduction in the degree of toxæmia, but this was not the general experience. Various reasons are offered by Parsons which might explain why the results obtained differed from those reported by McSweeney, and it is not suggested that the effectiveness of the method is finally disproved. In any case, the conclusions apply only to 'typhoid fever as it occurs in the Middle East'. However, the main conclusion reached is worth quoting in that it suggests some essential practical points in evaluating the method anywhere; it is that the treatment 'would have to produce much more dramatic results in the way of a rapid cure of the illness if the disturbance to the patient of repeated injections was to be counter-balanced'.

Control of Thyreotoxicosis by Methyl Thiouracil

By H. R. G. POATE

(Abstracted from the *Medical Journal of Australia*, Vol. 2, 26th July, 1947, p. 93)

METHYL THIOURACIL is superior to other 'thio' preparations in the treatment of thyreotoxicosis.

The minimal dose which will produce the desired effect is the safest dosage.

Each patient presents an individual problem and requires constant supervision during the whole course of treatment.

The major factor in securing permanency of control of thyreotoxicosis in the maintenance of a zero or minus metabolic rate for four months before cessation of treatment.

Adjuvant therapy in the form of sedation, mixed vitamin therapy and adequate balanced diet is necessary.

A high protein diet is necessary if there has been any undue loss of weight or muscle wasting.

Regular leucocyte counts are imperative, and if possible estimation of the basal metabolic rate for the first six to eight weeks are advisable. Follow-up should be carried out for six months after treatment is suspended.

The final period of treatment should be five months if *Thyroideum siccum* has been given, and if so it should be six months.

The best results are obtainable in cases of acute hyperplastic toxic goitre, and the earlier the patients come to treatment, the more satisfactory is the final result. Present figures indicate that apparent cure can be obtained in 88 per cent of cases when the technique as outlined is followed faithfully.

Gland hyperplasia and exophthalmos of moderate degree can be cleared in most cases of not more than four months' duration by the administration of *Thyroideum siccum* during the maintenance period of dosage.

Patients with toxic adenomatous goitre do not respond satisfactorily to this form of treatment, and if operable should be advised to have surgical treatment as soon as control of toxicity is secured. It is necessary in all such cases to have a Quick's hippuric acid excretion test carried out to determine the detoxicating function of the liver which is depressed in so many of these cases, rendering operation a risky procedure.

The previous administration of iodine doubles the average time to secure 'adequate response' and lengthens the total period of time for treatment.

Mild idiosyncratic reactions may occur, but seldom necessitate suspension of treatment for more than twenty-four to forty-eight hours.

Febrile reactions should be regarded as a warning of a more severe toxic reaction. Leucopenia should also be regarded with suspicion, as agranulocytosis, although rare, must always be kept in mind.

Only two cases of relapse some months after cessation of treatment have been observed—one with thiouracil and one with methyl thiouracil, that is, less than 2 per cent in the combined total.

Misuse of 'thio' drugs is still found, and they should not be ordered without a proven diagnosis of thyreotoxicosis as they are valueless in neuroses which may mimic thyreotoxicosis closely.

What to do in Case of Venous Air Embolism

(From the *Medical Journal of Australia*, Vol. 2, 2nd August, 1947, p. 147)

VENOUS (or pulmonary) air embolism is a rare uncommon occurrence; but it is a most alarming one and often fatal. Air may enter the systemic vein in sufficient quantity to produce serious embolic effects in the course of a number of different surgical procedures: such are operations in which large veins of the head or neck may be opened, and diagnostic procedures in which air is injected, as when gas or air is insufflated through the uterine tubes to test their patency, or round the kidneys for x-ray examination of the suprarenal glands. There is a similar danger during vaginal insufflation with a powder blower and during obstetrical operations in which a hand is intro-

duced into the uterus, also during various other less common surgical manœuvres. It is a not uncommon cause of death during attempts to procure abortion by injection of foreign substance into the uterus with a syringe.

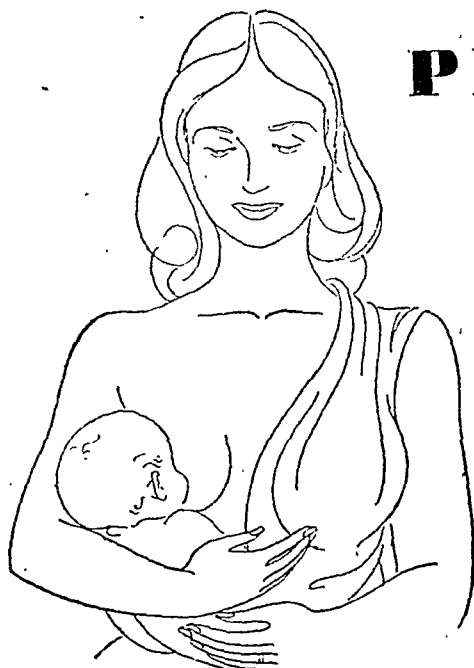
T. M. Durant, of Philadelphia, and his collaborators have made experimental studies of venous air embolism in the dog. Under anaesthesia air was injected intravenously during the experiments, and in some of the animals the thorax was laid open so that the heart could be observed. It was found that a quite large quantity of air might enter a vein without causing serious trouble, provided that it did not enter too rapidly. This is very different from what happens with arterial air embolism, in which very serious peripheral effects may be caused by a minute bubble of air. It appeared also from the experiments that it is possible for a certain amount of air entering the veins to be transported to the lungs and there to be excreted from the circulation, a process accompanied by tachypnoea. When death occurs from venous air embolism, it is due to circulatory obstruction resulting from an air lock in the path of outflow from the right ventricle. The right ventricle in this region becomes dilated and ischaemic. It is in this connection that the authors have made their most important discovery. If the animal is turned on to its left side, the air forming the lock floats away from the outflow tract and takes up another position. Forceful contractions of the right ventricle are very quickly resumed and the pulmonary circulation is restored; the air in the ventricle is presumably churned into a froth which gradually passes out into the lungs where the air is excreted from the blood stream.

This work of Durant and his collaborators should be applicable to man; if it is, we now possess a logical form of treatment, capable of immediate application and with dramatic effect, for a catastrophe that hitherto placed the sufferer in imminent peril of death. No longer need precious moments be wasted on injections of analeptics or of stimulants for a heart that is doing all it can. The patient will be turned on to the left side.

Vitamin C Deficiency Simulating Acute Abdominal Emergencies

(From the *Medical Journal of Australia*, Vol. 2, 1st November, 1947, p. 552)

THE classical signs of scurvy are rarely seen in this country, though there must be a good many individuals who for various reasons receive an inadequate amount of vitamin C. Opinion differs as to the frequency of occurrence and the importance of subclinical scurvy; but it seems worth while to draw attention to three cases, recently reported by Laurence E. Hines of Chicago, of subperitoneal hæmorrhage from vitamin C deficiency, which simulated in its effects acute surgical abdominal conditions. The first instance was in a youth, who was kicked in the abdomen during a football game. Thirty minutes later he vomited and developed pain in the upper part of the abdomen, which steadily increased until it became unbearable. The presence of a ruptured viscus was suspected, and laparotomy performed. An 'enormous number' of ecchymotic and petechial hæmorrhages were found, covering almost the entire mesentery, with a few hæmorrhages scattered over the anterior surfaces of the ileum, jejunum and cæcum; no other abnormality was present in the abdomen. The ascorbic acid level of the patient's plasma was found to be 0.3 milligramme per centum (normal value is 0.5 to 2.0 milligrammes per centum) and the carrying out of a capillary fragility test on the arm resulted in the appearance of numerous petechiæ. Investigation of the patient's diet showed a very poor intake of foods containing



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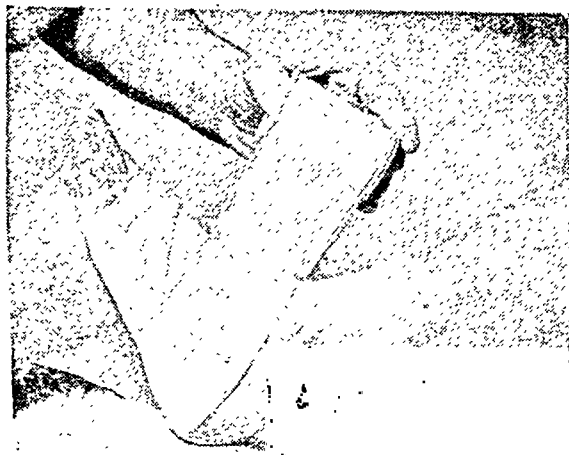
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vitamin C. He recovered uneventfully with administration of an adequate diet and ascorbic acid given parenterally. The second patient, a middle-aged man, had pain in the right lower quadrant of the abdomen of spontaneous onset and of four days' duration. He had no nausea or vomiting, but the physical signs were consistent with a diagnosis of acute appendicitis. At operation the greater omentum, thick and indurated, was found adherent to the anterior part of the parietal peritoneum. The parietal subserosa at the site was extensively infiltrated with hemorrhage and the omentum was thick and purple. Microscopic examination of the omentum revealed fatty tissue with hemorrhage between fat cells and considerable hyperemia of the blood vessels. The ascorbic acid level was 0.6 milligramme *per centum* and a positive result was obtained to the capillary fragility test. The patient seldom ate citrus fruits or vegetables and took from four to ten drinks of whisky each day. The third patient, a woman, aged thirty years, had had severe abdominal pain for five hours with vomiting. Physical examination revealed extreme tenderness and board-like rigidity of the abdomen with only occasional peristaltic sounds. Bowel obstruction or perforation of a viscus was suspected; but since ordinary percussion of the chest and palpation of the muscles of the back and extremities revealed great tenderness and because of the lack of leucocytosis, surgical exploration was postponed. Twenty-four hours later signs of tetany appeared. Low levels of vitamin C, calcium, phosphorus and total protein and fatty turbid serum were found on blood examination. Intravenous administration of calcium controlled the muscle pain and spasm, and prompt improvement in clinical and laboratory findings followed administration of an adequate diet supplemented with vitamin C and the B complex, as well as liver extract. The patient was found to be a chronic alcoholic who during a recent debauch had taken no food for several days.

It seems clear that in these three cases, despite other factors present, the clinical condition was essentially due to vitamin C deficiency. Diagnosis of such a state cannot always depend upon the classical clinical findings, but laboratory investigation should reveal it. The effects described are probably too uncommon for the condition to figure prominently in the differential diagnosis of the acute abdominal emergency and it would need to be very firmly established to counterbalance other indications in favour of surgical interference. Just the same, it is as well to know that it does occur.

Induced Pyrexia

By H. HALES

(Abstracted from the *Medical Press*, Vol. 218,
10th December, 1947, p. 538)

As American workers have shown, the optimum rectal temperature should be 106°F. or more, and this should be maintained for six to eight hours. In the United States air-conditioned cabinets and ultra-short-wave diathermy are the favourite methods. My own experience confirms this choice, but good results can be obtained by using ultra-short-wave diathermy combined with electric blanket, and cabinets are not essential.

The temperature is more easily controlled by electropyrexa and can usually be raised to a higher level than with malarial therapy; the element of infection with a parasite and need for an antidote is obviated. The only drawback is the need for skilled assistants and expensive apparatus, but the results appear to justify this.

A New Treatment for the 'Lightning Pains' of Tabes Dorsalis

By R. T. COTELLO

(Abstracted from the *Urologic and Cutaneous Review*, Vol. 51, May 1947, p. 260)

THE type of treatment which the author has been using at Wayne County General Hospital for the past seven years seems to offer more consistent chances of success than anything used previously. 'Protamide' under the old name of 'protozyme' was first put on the market about eighteen or twenty years ago when tissue extracts were having one of their periodical returns to favour. It was a proprietary preparation and in common with many of these preparations it was advertised as somewhat of a panacea.

Among the many conditions which it was alleged to benefit was tabes dorsalis. It had a mild popularity for a while but like most cure-alls its results were disappointing in general and it fell into disrepute, aided perhaps by the fact that it occasionally and unpredictably gave very severe reactions. The present study was started about seven years ago, and except for occasional interruptions due to the war has continued to the present time. The majority of the patients were treated at Wayne County General Hospital under the supervision of the author. Samples were also sent to various neurologists throughout the country and their results have also been incorporated in this report. The author's patients were selected on the basis of a long history of tabes dorsalis with lightning pains; most of the patients selected had had many years of anti-syphilitic treatment. All had a definite and unmistakable clinical picture of tabes dorsalis, some had a persistent positive serology in the blood or spinal fluid although many, after years of treatment, had negative serology but persistent symptoms. Many of the patients selected had been residents at the hospital for many years and so could be observed over long periods of time.

A study of the preparation used is of interest. In its original form protamide (protozyme) was a sterile colloidal solution of processed and denatured proteolytic enzyme (pepsin)—obtained from the glandular layer of fresh hog stomach—prepared by incubating the pepsin in a water-bath at rigidly controlled temperatures for a definite length of time. This solution was mixed in proportions of 12 cc. of the pepsin solution with 4.6 gr. sodium salicylate and 9.2 gr. sodium iodide in 10 cc. of sterile distilled water. The solution was intended to be given intravenously at the rate of 1 cc. per minute. Early in the study it was found that many patients developed reactions, either from sensitivity to the iodine in the preparation or, if given too rapidly, a histamine-like reaction with headache, flushing of the face, etc. It was suggested that the enzyme alone, without the iodine and salicylate, be prepared for intramuscular use. This was done and was found to be just as efficacious as the previous mixture with no appreciable toxic results. This latter preparation is the one which is now marketed under the name protamide.

The pharmacology and toxicology of protamide was investigated by Dr. Fritz Yonkman and associates at the Department of Pharmacology at Wayne University College of Medicine. They found that rapid intravenous injections in rats and rabbits produced severe anaphylactoid reactions but slow injections were relatively non-toxic. Prolonged administration had no effect on general health and growth curves. The production of protein sensitivity and true anaphylaxis could be demonstrated in guinea-pigs. The haemodynamic actions of the extract were typical of those produced by tissue extracts in general.

The intramuscular preparation is only moderately painful, considerably less so than an equal volume of injectable thiamin chloride.

Treatments were given once a week over varying periods of time. Only those of the author's cases are reported in which treatment was continued for at least four weeks. Fifty patients were followed for long enough period of time to draw definite conclusions. In addition, thirty-nine cases are reported treated by other men to whom supplies of protamide were sent for clinical trial.

In two groups of patients—one group of fifty and the other of thirty-nine—complete relief from pain was obtained in 52 per cent and 41 per cent respectively, slight to moderately relief in 38 per cent and 41 per cent, and no relief in 10 per cent and 18 per cent respectively.

Pharmacologic and toxicologic tests on animals showed anaphylactoid reactions on rapid intravenous injection but none when administered slowly. Protein sensitivity and true anaphylaxis could not be produced.

A course of treatment of twenty weekly injections is suggested as a preliminary treatment with additional injections as indicated.

Antibacterial Therapy and the Balance of Nature

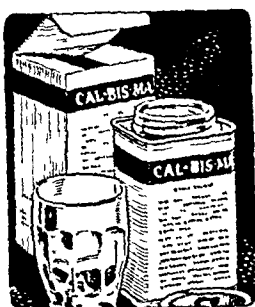
(From the *Medical Journal of Australia*, Vol. 2, 20th December, 1947, p. 755)

THOSE who probe Nature's secrets know that she does not suffer fools gladly. The balance of nature is no myth, a fact unpleasantly evident from such problems as soil erosion and the control of atomic energy. In this regard, perhaps too little respect is shown to some of the powerful agents made available by modern medicine. The manifest association between androgenic substances and carcinoma of the prostate has not completely curbed clumsy interference with the body's delicate hormonal balance. The attitude towards the sulphonamides has progressed only slowly from one of confident enthusiasm to one of uneasy caution. In addition to the dangers of sensitization, so little appreciated at first, striking evidence was published last year of their capacity to upset the balance of bacterial action in the bowel. It may be remembered that S. W. Hardwick reported a case of acute nicotinamide deficiency developing suddenly in a patient who was treated with sulphaguanidine for acute dysentery of the Flexner type. He quoted the work of P. Ellinger who had previously demonstrated experimentally that the administration of succinylsulphathiazole by mouth was followed by a drop in the urinary output of nicotinamide of the order of 60 per cent. It appeared nicotinamide was synthesized and released by bacterial action in the gut and from there absorbed into the blood stream. The experimental or therapeutic administration of the so-called 'sterilizing' sulphonamides had interfered with this biosynthesis. Hardwick suggests that there may be organisms which produce nicotinamide and others which destroy it; the sulphonamides by a selective sterilizing action upset the balance in favour of the second group. Later, a report appeared from Ellinger and F. M. Shattock of two cases of nicotinamide deficiency, one following oral intake of sulphadiazine and the other after oral intake of penicillin. In both cases symptoms disappeared after discontinuance of the drugs and administration of nicotinic acid.

Another interesting aspect of this general problem has been recently brought forward by Louis Weinstein in relation to the antibiotic drugs, penicillin and streptomycin. He refers to the specificity of the antibacterial action of these agents and reports the development of new infections due to non-susceptible organisms during the course of treatment with one or the other.

These new infections may arise either from organisms already present, for example, in the nose and throat, or from organisms introduced in the very act of administering the antibiotic. Five detailed case reports are given. One patient had extensive diphtheria and from his nose and throat swabbings cultures of haemolytic *Staphylococcus aureus*, *Corynebacterium diphtheriae* and type 14 pneumococcus were grown. Penicillin was administered (as well as diphtheria antitoxin). From the fourth day after the patient's admission to hospital large numbers of *Klebsiella pneumoniae* and *Escherichia coli* were found in the sputum and throat, and though the original infection had responded to treatment the secondary invaders (which were, of course, not susceptible to penicillin) caused death. Another patient, a child with a probable diagnosis of atypical pneumonia of virus origin, was treated with penicillin. On the fourth day after the patient's admission to hospital *Haemophilus influenzae* was grown from throat swabbings in almost pure culture for the first time; it was later recovered from the blood. Administration of streptomycin brought an immediate response. Later, the temperature again rose as signs of inflammation appeared at the site of a needle puncture, but re-introduction of penicillin therapy controlled this and the patient recovered after a period of treatment with the two drugs simultaneously. Three other patients were treated with streptomycin for *Haemophilus influenzae* infections. One developed broncho-pneumonia with bacteraemia, another meningitis with bacteraemia and a third recurrent pyelonephritis, all caused by haemolytic *Staphylococcus aureus*. Weinstein states that the mechanism by which such infections occur is not clear. However, in four of the patients there was a remarkable change in bacterial flora in the nose and throat before new infection developed. Organisms that were apparently present in such small numbers that they were not detected early in the course of the disease increased in number after treatment with penicillin or streptomycin and invaded the tissues. Weinstein suggests that in some persons a high degree of bacterial antagonism may exist in areas like the naso-pharynx and that certain groups of bacteria are kept in check by others. The specific antibacterial action of penicillin or streptomycin may upset this balance, and those organisms that are unaffected by the drug will increase sharply in number and possibly in virulence. This raises the question of the use of these drugs in the absence of an exact bacteriological diagnosis. This may be not merely without effect, but actually harmful. For example, the treatment of virus infections with streptomycin or penicillin may be dangerous because these drugs have no effect on the primary disease, and they may allow organisms that are normally present in various tissues and are not susceptible to their action to grow profusely and to invade the tissues. Careful bacteriological studies are important both before the commencement of treatment and also during its course. An increase in numbers of an organism in the naso-pharynx frequently precedes its invasion of the tissues by at least twenty-four hours. The discovery of a preponderance of *Haemophilus influenzae* or of *Staphylococcus aureus* in the naso-pharyngeal flora during the course of penicillin or streptomycin treatment should put the medical attendant on guard against a complicating infection, particularly if the patient is a young child. Weinstein considers that the use of streptomycin and penicillin together at the beginning of an infectious disease, especially as a substitute for bacteriological investigation, is to be described. Apart from the quite unintelligent nature of such therapy there is a danger of the patient's developing sensitivity to a drug which is being used unnecessarily and so being denied the benefit of its use when it may be indicated later on.

None of these problems are insuperable if they are appreciated. Indeed, their occurrence may not be entirely to be bemoaned if they encourage intelligence in the use of powerful agents and respect for the balance of nature.



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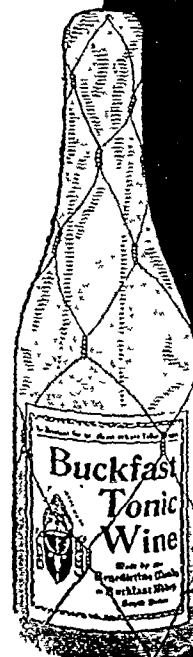
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Loose versus Close-Fitting Clothing for Work in 'Tropical Heat'

By C. P. YAGLOU

and

M. N. RAO

(Abstracted from the *Tropical Diseases Bulletin*, Vol. 44, July 1947, p. 677)

Tests were carried out during the war on behalf of the National Research Council of America with close-fitting and loose-fitting clothes, the experiments were done in a room with air and walls at 85°F., and with a relative humidity of 85 per cent. The speed of air movement relative to the subjects was about 70 ft. per minute. The three subjects—healthy men—performed step-climbing at a rate which called for an energy expenditure of 255 calories per hour. Work was done for 25 minutes in each half-hour for a period of at least 4 hours.

The close-fitting garments used were 80/20 cotton-wool knitted union suits, chosen to fit each man individually, and of an average weight of 480 gm. The loose-fitting garments were two-piece cotton pyjamas weighing 320 gm. The tests on these garments were carried out during winter, and during the following summer, further tests were made on the 'Quartermaster-General' poplin jungle suit. This latter garment was tested with the trouser legs and the collar open (ventilated) as well as closed (unventilated). Further tests were made with the subjects unclothed.

All the men felt cooler and less tired during and after work in the experiments done without clothing. They disliked working in the close-fitting union suit and in the unventilated jungle suit, because they became damp and sticky as well as too warm. Adherence of wet clothing to the skin was objectionable. The loose-fitting pyjama suit was the coolest garb. The ventilated jungle suit also remained mostly dry. Similar results were shown by the objective measurements, especially the rate of sweat production.

It is concluded that in tropical heat the rate of sweat secretion during work is a better index of the heat discomfort than is the pulse rate of the rectal, skin or mouth temperature. When solar radiation is no problem, any clothing is a hindrance to body heat loss, and if clothing must be worn it should be loose-fitting and of light weight. It should be designed for maximum ventilation and should expose as much skin area as possible. Clothing should be designed to give ventilation by bellows action. The closing of the jungle suit to keep out mosquitoes imposes considerable heat strain on the wearer.

Treatment of Myasthenia Gravis

(Abstracted from the *Lancet*, i, 5th April, 1947, p. 453)

THE neuromuscular defect in myasthenia gravis has been the subject of much research in the last few years, and its mechanism is becoming clearer. Clinical observation suggested that the essential defect was in transmission at the myoneural junction. There were three possible reasons for the interruption—too little acetylcholine might be produced; the acetylcholine might be destroyed abnormally rapidly by cholinesterase; or some substance similar in action to curare might block the action of acetylcholine.

When prostigmin was found to be effective by mouth, though the dose was considerably larger than by injection, a new era opened for the sufferers from this disease. In many patients, however, increasing doses had to be given, and in some the myasthenic symptoms were not properly controlled even by large doses. A new drug—di-isopropyl-fluorophosphate

(DFP)—which inhibits cholinesterase activity has recently been introduced at the University of Pennsylvania. The effects are notably less than with prostigmin, while larger doses of DFP causes nausea, vomiting and faintness which are not adequately controlled by atropine. The main advantage of DFP is that its action lasts much longer than that of prostigmin, and a combination of the two drugs might at times be helpful in treatment.

Surgery offers an alternative approach. It was an old observation that cases of myasthenia gravis sometimes showed tumours of the thymus at autopsy. There is no doubt that thymectomy is a real advance in treatment, especially in the younger patients with a relatively short history. In Paris a new surgical treatment has recently been . . . denervation of the carotid sinus. . . . extracts have been thought to improve the symptoms of myasthenia, and this operation is supposed to cause hyperplasia of the suprarenal cortex.

Prognosis in Erythroblastosis foetalis

(Abstracted from the *Lancet*, i, 5th April, 1947, p. 457)

WALLERSTEIN reported cases of severe erythroblastosis successfully treated by removal of the blood of the new-born infant and its replacement with Rh-negative blood.

His original technique was to remove the infant's own blood by fontanelle puncture of the longitudinal sinus and to transfuse Rh-negative blood into a cannulated arm vein. He infused 75-100 c.cm. more blood than had been removed. Wiener and Wexler have found that, by heparinizing the infant with 500 units intravenously and cannulating the cut radial artery, they could remove through a 20-gauge needle 150 c.cm. of blood before clotting occurred in the radial cannula; by giving a further 500 units of heparin it was possible to remove a total of 400 c.cm.

The procedure is readily practicable and satisfactory when the diagnosis is made early, and offers many advantages over simple transfusion with Rh-negative blood. The general impression of paediatricians is that the mortality from this disease is still around 50 per cent and that in the infants who survive damage to brain and liver may be manifested later.

Both Wiener and Wallerstein, though they have made notable contributions to paediatric practice by evolving this technique of exchange transfusions, may be raising unduly high hopes. First, the treatment must be given very early. Secondly, both appear to lay too great a stress on the damage to the infant in extra-uterine life. That damage also occurs in intra-uterine life is evidenced by the high proportion of stillbirths in cases of Rh blood-group incompatibility between mother and infant with maternal iso-immunization. If the foetal tissues contain the Rh antigen, as has been demonstrated by Boorman and Dodd, the tissue cells as well as the red cells will be damaged by the maternal antibody. In the long run, therefore, the greatest promise will be held out by a regime which will prevent the maternal antibody from being formed or from passing across the placenta to damage the infant.

Salmonella Enteritidis Infection Associated with Use of Anti-Rodent 'Virus'

By J. G. DATHAN *et al.*

(Abstracted from the *Lancet*, i, 24th May, 1947, p. 711)

In a household of five children and three adults, a 'virus' preparation was used three times for the extermination of mice. About ten days after its last

use some members of the household were found to be infected with *Salmonella enteritidis*.

The organism in the virus preparation was identical with the one isolated from the patient. It was *S. enteritidis* var. *gent*.

Injectons. without Needles

(Abstracted from the *Lancet*, i, 24th May, 1947, p. 732)

A DETROIT engineer has invented an instrument for injecting solutions directly through the skin. The apparatus is a metal cylinder about the size of a flash light, with a powerful spring inside. The ampoule containing the solution is fitted into the end of the cylinder and this is placed on the patient's arm. The doctor then presses the button and the solution, forced through a hole $1/300$ inch in diameter at a pressure of 3,200 lb per sq. inch, passes through the skin in a fraction of a second, causing no pain. The idea of the apparatus came from the observation that oil from diesel engine jets often penetrates the skin of engineers.

The Ætiology and Modern Treatment of Achlorhydria

By J. RONALD

(Abstracted from the *Medical Press*, Vol. 219, 2nd June, 1948, p. 479)

It is essential to establish whether or not a condition such as pernicious anaemia or carcinoma is associated with the achlorhydria, and for this the aid of special methods of investigation must be sought. The clinical findings must be carefully considered as well as the results of ancillary investigations.

General—If the patient is symptom-free, and the discovery of achlorhydria made accidentally, no special treatment is required. If investigations, when symptoms are present, reveal no evidence of serious underlying trouble, the case should be treated on the assumption that gastritis is the ætiological factor requiring attention. Treatment should not be neglected, as it may be of value in preventing the onset of serious complications.

The teeth should be examined, both from the point of view of sepsis and of efficient mastication. Unsatisfactory dentures should be remodelled. Dental sepsis should be actively treated and other foci of infection eliminated, particularly in the upper respiratory tract.

Alcohol should be forbidden in the early stages but may later be allowed with meals; cocktails and 'short drinks' should, however, be entirely given up. Smoking may be permitted in moderation, but is better dispensed with initially.

Diet—In the early stages, diet should be light, nutritious and easily digested; hence it should as far as possible be broken up and given in liquid or semi-solid form. Food should be adequately chewed. Soups and puréed vegetables are well tolerated, as are well-cooked potatoes. Eggs are best given soft-boiled. Fish, chicken or rabbit may be given, and small amounts of sweet-breads or finely-minced meat. Milk may not be well borne, but is often acceptable if citrated, flavoured or diluted with potash or soda water. As the appetite improves, additions can be made to the diet. Crisp toast, Ryvita, etc. are valuable in that they tend to stimulate salivary gland secretion.

Mechanical.—In the early stages, considerable benefit may be obtained from gastric lavage in the morning before breakfast. Weak hydrogen peroxide (ten vols) in the proportion of one to two drachms per pint of water is an efficient agent in clearing the stomach of mucus and debris. The lavage may be accomplished by means of a Senoran's evacuator or by tube and funnel. Many patients can be taught to carry out the manoeuvre themselves. It should be continued daily until the returned washings are clear. In practice, satisfactory results are usually obtained in one or two weeks, but it may be advisable in some cases to continue for longer periods.

If it is undesirable for any reason to institute this regime, an alternative is the drinking by the fasting patient of a tumblerful of warm water containing a drachm of sodium bicarbonate: this is often perfectly adequate.

Drugs—If, after adoption of the above measures, there is not evidence of return of free hydrochloric acid to the gastric juice, hydrochloric acid should be exhibited. This is best given with meals, flavoured with orange or sugar, in doses of one drachm of dilute hydrochloric acid (B.P.) to four ounces of water. This provides a fluid of 0.3 per cent concentration of acid, which is approximately the concentration found in normal gastric juice. As the acid has a destructive effect on the teeth, it should be taken through a glass tube or straw, and the mouth rinsed with plain water after each meal. The taking of hydrochloric acid by mouth has been shown to inhibit the secretion of pepsin, and it is unusual to prescribe pepsin in three- or five-gram doses, either in tablet form or as glycerine of pepsin in a mixture with the acid.

In cases where the tongue and mouth are sore, it may be found that the administration of hydrochloric acid in solution causes pain. In such circumstances certain proprietary preparations in tablet form may usefully be employed, e.g. acidolpepsin (Bayer), acidulin (Lilly), or akloiepe (Roberts).

Bitter tonics taken before meals may prove of value (nux vomica, rhubarb, gentian), and are best given with an alkali. This apparent paradox is probably explained by the fact that the alkali will ensure neutralization of organic acids; it can be omitted as improvement takes place.

If evidence of carbohydrate dyspepsia or fermentation is found, takadiastase (P.D.) may prove of value, either alone or in combination with pepsin or pancreatin.

Diarrhoea, if present, will usually yield rapidly to the administration of hydrochloric acid. More commonly there is constipation, which may be overcome by means of salines and aperient waters. A substitute for Carlbad water may be made with one drachm of sodium phosphate in half a pint of water. Senna or cascara should be used, if required, rather than the stronger purgatives, but an occasional mercury pill may help. Gentle abdominal massage may be given.

The use of mild sedatives may be indicated in the presence of nervous factors.

Should a specific lesion be identified in association with the achlorhydria, further treatment will obviously be required. In the macrocytic anemias, liver or possibly folic acid is indicated; in the microcytic anemias iron. It is worthy of note that iron should be given in large doses as absorption is poor in the achlorhydric stomach; assimilable and non-irritant preparations should be used, e.g. ferrous sulphate or collonon (Evans). Surgical measures may be called for if neoplasm or cholecystitis is found.

The fact that achlorhydria is not a disease should never be forgotten. When no definite cause is identified, the physician should not allow himself to drift into a position of false security but should maintain a watching brief for possible future developments.



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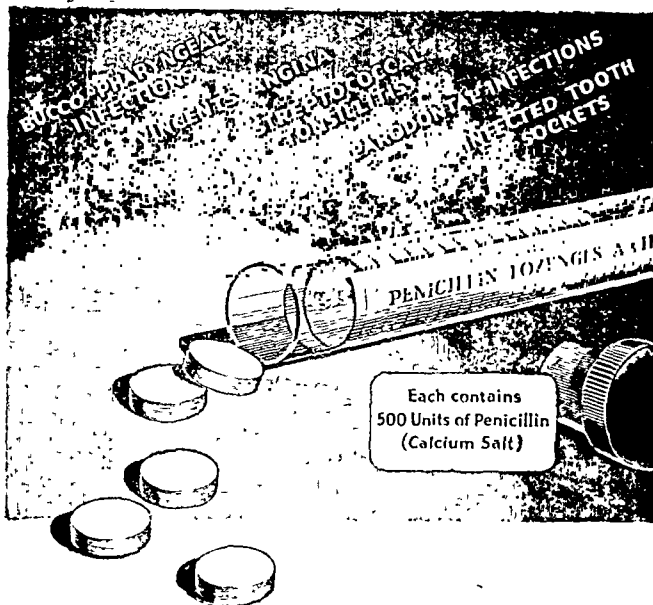
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Reviews

PRE-OPERATIVE AND POST-OPERATIVE CARE OF SURGICAL PATIENTS.—By H. C. Ilgenfritz, A.B., M.D., F.A.C.S. 1948. The C. V. Mosby Company, St. Louis. Pp. 898. Illustrated

THE author has taken great pains in getting together nearly all the factors that need attention in the care of patients under surgical treatment. The volume will be particularly useful for house surgeons and younger surgeons who need definite opinion of more experienced men and there is hardly any element left out from the book, which may be of use to them. Details of procedures are of great value. The discussions on various physiological and pathological processes add to the value of the book.

L. M. B.

ABDOMINAL OPERATIONS.—By Rodney Maingot, F.R.C.S. (Eng.). Second Edition. 1948. H. K. Lewis and Company, Limited, London. Pp. xxiii plus 1274. Illustrated. Price, 84s.

A SECOND EDITION of this book has been greatly improved and much new matter added. The value of the book rests in the well-expressed opinion on the merits of different methods of procedures of surgical measures with the weight of personal experience. The volume is copiously illustrated and is written in a lucid and authoritative manner.

L. M. B.

CANCER OF THE OESOPHAGUS AND GASTRIC CARDIA.—Edited by G. T. Pack, B.S., M.D. 1949. The C. V. Mosby Company, St. Louis. Pp. 192. Illustrated

A VERY well-written book of the more modern method of dealing with cancer of oesophagus and gastric cardia. It describes the procedures in such a convincing way that the older operations are relegated to obsolete methods. The transthoracic combination when properly done means a great difference to the comfort of the patient and subsequent enjoyment of life.

L. M. B.

DISEASES OF THE NOSE AND THROAT: A TEXT-BOOK FOR STUDENTS AND PRACTITIONERS.—By Sir St. Clair Thomson, M.D., F.R.C.P. (Lond.), F.R.C.S. (Eng.), LL.D. (Hon.), and V. E. Negus, M.S. (Lond.), F.R.C.S. (Eng.). Fifth Edition. 1948. Cassell and Company, Limited, London. Pp. xix plus 1004. Illustrated. Price, 70s.

A NEW edition of this valuable work is very welcome and though the actual size is not much altered the contents have been revised, re-written and new material has been added to make it up to date. The chapters on neurological affection and malignant growths are more easy to read and understand. Every surgical procedure is given minute detailed directions making them useful to the younger surgeons. The illustrations are copious and instructive and help considerably to follow the text.

L. M. B.

PASTEURIZATION.—By H. Hill, F.R.San.I., A.M.I.S.F., F.S.I.A. Second Edition. 1947. H. K. Lewis and Company, Limited, London. Pp. viii plus 297 with 73 Illustrations. Price, 21s.

THIS well-written book emphasizes the technical and engineering aspects of the design and operation of pasteurization plants and furnishes valuable information on many details not ordinarily found in books.

The author has drawn attention to the dangers of flash pasteurization. His remark 'Short time process plants have to operate with an exceedingly small safety margin' deserves to be pondered over by the health authorities in our country, as the initial bacterial content is high in our milk. Sterilized milk is at least safe. Details of other processing methods, bottling, cleaning laboratory control, etc., have been furnished.

K. S.

A. TEXTBOOK OF GYNÆCOLOGY.—By Wilfred Shaw, M.A., M.D. (Cantab.), F.R.C.S. (Eng.), F.R.C.O.G. Fifth Edition. 1948. J. and A. Churchill Ltd., London. Pp. vii plus 660. Illustrated. Price, 25s.

THIS is a textbook presenting an up-to-date account of gynæcology for students. Mr. Shaw is well known as a renowned teacher. Those of us who had the privilege of attending his clinics know him as one who is always very helpful in explaining the difficulties that face a student in the course of his studies in obstetrics and gynæcology. This book is written in the pleasant and easily comprehensive style which is Mr. Shaw's very own. It is very difficult to single out any section of the book for special appreciation. As the reviewer always has a special regard for Mr. Shaw's contribution in gynæcological pathology, he has been specially attracted towards the sections dealing with the pathology of difficult topics, e.g., Functional Uterine Bleeding, Ovarian Tumours, Carcinoma of Uterus, etc. The anatomy of Prolapse of Uterus has been dealt with in a useful and elaborate way. Readers of the *British Medical Journal* are aware of the new conception of the subject as described by the author.

Masters of any line of thought often make statements which appear dogmatic. Mr. Shaw cannot escape criticism on this account. On page 302 he states: 'It is impossible for the operator to reach the fundus of the uterus, etc.'. 'It is not impossible', most of us would say that. Intra-uterine douches have been advocated in the routine evacuation of the uterus. One thinks this is not only not necessary but is also a dangerous practice to adopt in many cases. While operating in an urgent case of tubal rupture one seldom finds it difficult to detect the affected tube though the author on page 333 has warned the reader of such a difficulty.

The get-up and printing of the book is in keeping with the usual high standard of Messrs. J. and A. Churchill.

M. N. S.

BOOKS RECEIVED

1. Chikitsa Jagat. Written in Bengali. A monthly Hospital Clinical Society, Jul. to November 1947. Published by the Editor from 27C, Upper Circular Road, Calcutta 9. Annual subscription Rs. 4. Price per copy: 6 annas only.

2. Proceedings of the Madras Government General Hospital Clinical Society, July to November, 1947. Edited by Dr. R. Subramaniam, B.Sc., M.D., M.R.C.P. (Lond.), and Dr. B. Ramamurthy, M.S., F.R.C.S. (Edin.).

3. India and the World in Medicine: A Synthetic Concept. By Dr. Pranjivan M. Mehta, M.D., M.S., F.R.C.P.S. Published by the Shree Gulabkuverba Ayurveda Society, Jamnagar. Pp. 44. Price, 'As. 12'.

Correspondence

CHANGES IN THE DOSAGE OF PALUDRINE

DEAR SIR,—In July of last year you favoured me with the hospitality of your correspondence columns to announce certain changes in the dosage of 'Paludrine'. Consequent on these changes in dosage it has become convenient to make available to the medical profession two new sizes of 'Paludrine' tablets. The availability of these new tablets is being announced this month in the medical press, but I shall be glad of the privilege of using once again your correspondence columns to inform the medical profession of the reason for introducing the new sized tablets.

The matter will be better understood, if I first recapitulate briefly the recommendations with regard to 'Paludrine' dosages :

(1) For protection against malignant tertian and suppression of benign tertian malaria—0.3 gm. once weekly, or 0.1 gm. twice a week at 3- and 4-day intervals.

(2) For radical cure of malignant tertian malaria—0.3 gm. twice daily for 10 days.

(3) In benign tertian malaria, the greatest hope of a radical cure with 'Paludrine' is offered by the dosage regime of 0.3 gm. daily until the fever subsides, and then 0.3 gm. once a week or 0.1 gm. twice weekly at 3- and 4-day intervals for about 6 months.

(4) For 'clinical' cure of all types of malaria—0.3 gm. daily until the fever subsides.

(5) For children over ten, the dosage for adults is indicated both for treatment and prophylaxis. Children under ten should be dosed according to age and size, but the minimum given to any child, however young, need not be less than 0.025 gm.

It is clear from the dosage schedules enumerated above that the most convenient dosage unit of 'Paludrine' is 0.3 gm. for adults and 0.025 gm. for young children. Tablets containing these quantities of 'Paludrine' hydrochloride have therefore been made available to the medical profession.

Yours faithfully,

J. M. MUNGA VIN, M.B., B.Ch. (Cantab.).
Medical Service Department,
I.C.I. (India), Ltd.,
Calcutta 1.

Any Questions

B.C.G. VACCINE TRAINING

SIR,—Be kind to impart your expert opinion on the point, whether persons holding L.M.F. and also D.T.M. qualifications are eligible for training abroad in B.C.G. vaccine, as mentioned in the column of 'Any Questions' in your esteemed journal.

Yours faithfully,

MAFIZUDDIN SIRKER.

P. O. TULSHIGHAT,
RANGPUR DIST.

[It is not clear what the writer means by 'training abroad in B.C.G. vaccine'. If it is the manufacture of B.C.G. vaccine, while there may be no great difficulty in obtaining the training, it is hardly likely that the manufacture will be permitted because the vaccine should be produced by an institution under Government control. In order to ensure uniformity in the potency of the vaccine, the production is also restricted to a single laboratory in each country. If it is training in administration of the vaccine, there is no need for any one to go abroad for the purpose. The six Scandinavian B.C.G. teams that are at present in India have come down to this country for the special purpose of training local doctors. They are at present

working in Amritsar, Baroda, Bombay, Calcutta and Madras. The sixth team is working in Colombo.—K. S. R.]

Service Notes

APPOINTMENTS AND TRANSFERS

THE undermentioned A.I.R.O. (M.) Officer is released from the army service and is granted the honorary rank of Major. His services have been placed at the disposal of the Government of India with effect from the date specified :—

ARMY IN INDIA RESERVE OF OFFICERS (MEDICAL)

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

Major Nanda Lal Mukherji. Dated 27th October, 1945.

THE undermentioned A.I.R.O. (M.) Officer relegated to Reserve on release from mobilized service, on the date shown against his name, is granted the honorary rank of Captain :—

ARMY IN INDIA RESERVE OF OFFICERS (MEDICAL)

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

Captain Sourendra Mohan Pathak. Dated 11th April, 1946.

LEAVE

Lieutenant-Colonel C. K. Lakshmanan, Director, All-India Institute of Hygiene and Public Health, Calcutta, is granted leave on average pay for 1 month with effect from the 24th January, 1949 (afternoon).

Publishers' Notice

SCIENTIFIC Articles and Notes of interest to the profession in India are solicited. Contributors of Original Articles are entitled to receive 25 reprints *gratis*; additional reprints can be obtained on payment. No reprints will be supplied unless contributors ask for them at the time of submitting their manuscripts.

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

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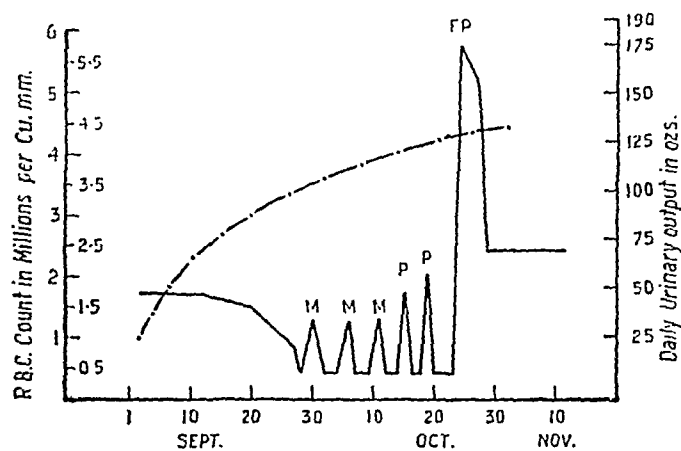
October, with similar results. On 26th October, she was given 'fortified plasma' containing 25 gm. of proteins. The diuretic response was dramatic. Her daily urinary excretion, which so far was in the region of 15 to 20 oz., shot up to 81 oz. on the day of transfusion, 183 oz. and 140 oz. on the succeeding two days. This continued at about 60 oz. daily for the next six days. As a result of this profuse diuresis, she was completely drained of her dropsy, except for a small collection at the ankles. On 3rd November, she went home against advice, and has never reported since.

Two features in this case are noteworthy :

(1) The œdema was completely refractory to mercurial diuretic.

CHART

CHART SHOWING ERYTHROPOIESIS AND DIURETIC RESPONSE.



M.- 1cc. of Esidrone Intramuscularly
P.- Plasma transfusion (12.5 gms. Protein)
FP.-Fortified plasma transfusion (25 gms. Protein)

(2) Owing to restricted supplies at the hospital, 250 cc., 250 cc. and equivalent of 500 cc. of plasma had to be given on 14th, 19th and 26th October, thus supplying 12.5, 12.5 and 25 gm. of protein on the three occasions. A brisk diuretic response of short duration was produced after transfusions on the 14th and 19th October, which did not affect the œdema materially. The transfusion on the 26th October produced a well-maintained diuresis, leading to disappearance of the œdema. Davies gave, in his case, a single transfusion containing 80 gm. of plasma protein and obtained satisfactory results. Given the initial plasma protein level, the amount of protein that ought to be transfused, can be accurately calculated, and in this calculation the following pertinent facts are noteworthy :—

Moore and Van Slyke (1930) have shown that the critical level of plasma proteins for the formation of œdema due to low intra-capillary osmotic tension is 5.5 ± 0.3 gm. per cent. Other factors like the blood electrolytes, blood

volume and the state of the capillary endothelium may, however, counterbalance the extra-capillary movement of fluids due to low osmotic tension due to hypoproteinæmia. Œdema therefore does not always occur when the plasma protein value is below the critical level. If the initial blood protein values are therefore known, the quantity of protein necessary to raise the blood protein above the critical level can be calculated, the volume of circulating plasma being known.

For every gramme of plasma protein formed, there is a corresponding change of 30 gm. in the tissue protein level (Sachan *et al.*, 1942). In cases of plasma transfusions in hypoproteinæmia, there is bound to be a very rapid movement of plasma proteins to make up tissue protein deficiency. An idea therefore can be obtained of the large quantities of proteins necessary to maintain a high blood protein level. This can be achieved by giving a high protein diet, say 150 gm. of protein daily.

The usual transfusion of 250 cc. of plasma is not enough; given at long intervals such transfusions should be ineffective.

A single large transfusion, with 80 gm. of plasma protein like the one used by Davies, is the ideal measure. The cause of failure in the case described by Das Gupta and Chatterjee (1947) is probably due to the administration of too little of plasma at too long intervals to have any effect on the plasma protein values and the œdema. We were however more fortunate in getting a satisfactory response in spite of the small quantities of plasma used.

Heathe and Taylor state that for the synthesis of 10 per cent, i.e. about 1.5 gm. of hæmoglobin, 80 gm. of body proteins are required. The erythropoiesis system obtains this from the store of tissue and plasma proteins. In the recovery phase of anæmias, hæmoglobin regenerates at a rate of about 0.1 gm. per day. This would consume about 6 gm. of tissue protein. Hence, high protein diets are most essential in these cases. Failure to attend to this detail would naturally lead to hypoproteinæmia with œdema.

One more point must be borne in mind in these cases. In the presence of severe anasarca, hæmoconcentration occurs and vitiates the value of the R.B.C. counts, hæmoglobin and plasma protein values, fairly high values being obtained. The usually rapid erythropoiesis noted in the cases mentioned by Holmes, Davies, Das Gupta and Chatterjee and ourselves are probably due to this factor. The presence of considerably hypoplastic bone marrow picture in our case lends further support to the view that the rapid rise in the R.B.C. count is not due to rapid erythropoiesis, but to the decrease of plasma volume. Unfortunately, the plasma volume has not been recorded in any of the cases referred to above.

Summary

A case of hypoproteinaemia during the recovery phase of anaemia is described.

The case well illustrates the rôle of osmotic tension in the formation of œdemas and also in the secretion of urine. The renal failure could not be corrected by mercurial diuretics. The correction of hypoproteinaemia by high protein diet and plasma transfusions resulted in profuse diuresis and rapid regression of œdema.

Regeneration of hæmoglobin, its effects on plasma protein and tissue protein, and theoretical considerations forming the basis of dietetic and parenteral therapy have been reviewed.

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OBSERVATIONS ON THE USE OF MYANESIN AS AN ANTICONVULSANT IN TETANUS

By AMALANANDA DAS, M.B., M.R.C.S. (Eng.),
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MYANESIN is the name given to B-dihydroxy-(2 methylphenoxy) propane. Its main action is that of a muscle relaxant. It has been claimed that it is only very slightly toxic.

Its chemistry and pharmacology were discussed by Berger and Bradley (Berger and Bradley, 1946, 1947). From these it appeared that it could antagonize strychnine convulsions which are due to heightened spinal reflexes, without causing loss of consciousness or muscular paralysis. There were no untoward side-effects like respiratory arrest or cardiovascular depression. These authors were also of the opinion that the drug did not have any cumulative action and was quickly destroyed in the body, and that it potentiated the action of barbiturate anaesthesia. Mallinson (1947) used

it in 112 cases of anaesthesia mainly with thiopentone and was of the opinion that it was capable of producing much better relaxation of abdominal muscles on a much lighter plane of anaesthesia. He gave the drug intravenously and found no toxic effect even when 50 cc. were injected in divided doses. It has since been used by several other anaesthetists.

The drug was first used in tetanus as a muscle relaxant by Belfrage in 2 cases (Belfrage, 1947). He used it intramuscularly every 1½ to 2 hours and gave 15 to 18 grammes daily. He did not find any toxic effects and reported satisfactory muscular relaxation. Other case reports on its use in tetanus have since appeared. Reports have also appeared that it could temporarily reduce spasticity in spastic muscular states due to upper motor neurone lesions, that it could temporarily check tremors of Parkinsonian syndrome and that it could stop epileptiform convulsions.

Adverse effects of the drug like venous thrombosis in the veins selected for injection, intravascular hæmolysis and hæmoglobinuria have been reported by Pugh and Enderby (1947). Hewer and Woolmer (1947) reported a case of death from renal anoxia. Cardiovascular depression was also noticed by the same authors after intravenous injections of myanesin.

The reports on its use as a muscle relaxant prompted us to use it in a series of cases of tetanus to enable us to assess its value. The present is a review of its action on 17 cases under the writers' observation.

There is a state of heightened spinal reflexes in tetanus. The muscular spasms fall into two categories. In the first category is the tonic contraction of the muscles of mastication producing trismus, of the muscles of the face producing risus sardonicus, of the muscles of the anterior abdominal wall producing rigidity, of the neck and spinal muscles producing stiffness and retraction of the head. Apart from this state of tonic contraction, there are paroxysmal exacerbations of the state of contraction of the muscles which are sometimes violent and may produce opisthotonos. These are sometimes due to external stimuli, or they may arise spontaneously. These will be referred to, in the absence of a better word, as clonic spasms.

Cases of tetanus were taken up for this observation at all stages when they were having frequent clonic spasms.

The muscular spasms of tetanus are painful and are a source of great distress and apprehension to the patient. Trismus interferes with speech and with the intake of adequate nourishment. They increase the demand on the energy resources of the body, cause a rise of temperature, and may produce death from respiratory arrest. The adverse psychological and physical effects of the spasms are great.

Suprapubic fistula closed on the 21st day. Patient walked away from the hospital on the 23rd day.

Case 11.—J., Hindu male, age 58, admitted for chronic retention five days old. Prostate moderately enlarged. B.P. 135/100 Hg. 80 per cent. Blood urea 45 mg. Urine: rbc ++, pus cells ++, albumin ++. One stage prostatectomy after urethral drainage for ten days. Profuse hæmorrhage during enucleation. Blood transfusion 250 cc. after operation. Patient expired same evening due to shock and hæmorrhage.

Case 12.—B. S., age 65, admitted for retention seven days old. Patient anæmic with swollen ankle and puffy face. Suprapubic cystostomy on 16th December, 1948. Blood urea 15 mg. Urine: albumin +, pus cells ++, rbc +. After the first stage patient's general condition improved. Œdema of ankles and puffiness of face subsided. Prostatectomy done on 6th January, 1949. On 25th January, 1949, suprapubic fistula closed. Patient is walking about and is about to be discharged.

Clinical features.—It will be noticed from these cases that symptoms of enlarged prostate start after the age of 55. The youngest patient was 58 and oldest was 78. Nine cases out of twelve were admitted for retention of urine, either acute or chronic (*i.e.* 75 per cent of cases); one case reported for repeated hæmorrhage and urgency and the others for dysuria and painful micturition. Although on being questioned these patients admitted that they were suffering from frequency, dysuria or urgency for some period but they overlooked the significance of those early symptoms. It must be remembered that symptoms of enlarged prostate may remain latent for years until the onset of acute retention. Symptoms of enlarged prostate start insidiously in three stages: first stage, stage of vesical irritation, *e.g.* frequency, second stage, stage of gradual obstruction, *e.g.* dysuria, third stage, stage of gradual renal failure.

In later stages complications like retention of urine, stone formation, epididymitis, cystitis, pyelitis, hæmorrhage, hydronephrosis, or malignancy may occur.

Frequency.—It is an early symptom, progressive and both nocturnal and diurnal. The nocturia is characteristic. Cause of this frequency is interpreted in different ways. In enlarged prostate the vesical sphincter is stretched when the urine leaks into the sensitive prostatic urethra before the bladder is full, there is a reflex act of micturition. Other causes given are enlarged middle lobe irritating the base of the bladder or disturbance of neuromuscular control brought by the changes in the bladder base. In later stages frequency is due to cystitis.

Dysuria.—The difficulty in passing water is of peculiar nature. The stream lacks force,

it starts feebly, gradually increase in power and falls away again to dribble at the end of micturition. The more the patient strains, the less he passes. How can this be accounted for? The unequal enlargement of lateral lobes or elongation of the posterior wall of the prostatic urethra produces distortion or kinking of the urethra, hence the difficulty in passage. Occasionally the middle lobe may act like a ball valve.

Urgency.—By urgency is meant the inability to retain water after the desire to micturate. The stretching of the internal sphincter of the neck of the bladder or trigonitis are probably the causes of urgency.

Retention of urine.—It may be partial, acute or chronic. Partial retention is due to the retro-prostate pouch, leading to *residual urine*. Residual urine is the amount of urine drawn by a catheter after the act of voluntary micturition. Acute retention is due to congestion at the bladder neck following pelvic congestion.

Hæmaturia.—Two cases out of 12 (16.6 per cent) reported for hæmaturia. It is not a common feature. It is mentioned recently that 'hæmaturia is a frequent and sometime the chief symptom of enlarged prostate'. Mostly it is due to instrumental disturbance during retention. Spontaneous hæmaturia is due to rupture of varicose vein at the base of the bladder or from erosion of enlarged prostate. It is not necessarily an indication of malignancy. Profuse hæmorrhage is more common in senile hypertrophy than in malignant prostate. In rare cases severe hæmorrhage occurs in the bladder leading to clot retention.

Pain is not an usual symptom. It is due to secondary complications like acute retention, trigonitis or calculus. Two of the cases suffered from pain, case 5 due to trigonitis and case 8 due to calculus.

Constipation is almost invariably present.

Sexual irritation may be distressing symptom.

Chronic uræmia is due to back pressure and renal damage.

Diagnosis.—Every man over 55 complaining of frequency and dysuria should be examined for enlarged prostate. On rectal examination the gland may feel as a large prominence in the rectum with firm elastic consistency and smooth surface with a median vertical sulcus. Enlarged prostate may not feel much enlarged per rectum. Cystoscopy is the final court of judgment. Normally the internal urethral orifice is seen slightly concave. When an intravesical enlargement is present, the convex rim like surface surrounds the orifice with V-shaped gaps between the different lobes. The prominent inter-uretic bar is marked in middle lobe obstruction, trabeculation and sacculation may be seen. Obstruction due to enlarged prostate should be differentiated from other causes of urinary obstruction: (a) Stricture urethra, (b) diseases

of the nervous system, *e.g.* disseminated sclerosis or tabes dorsalis, (c) bladder neck obstruction (median bar obstruction), and (d) vesical growth. The enlargement of the prostate due to age should be differentiated from other causes of enlargement: (a) Prostatitis, (b) carcinoma of prostate, (c) prostatic calculus, and (d) tuberculous prostate. Early age, history of gonorrhoea, nature of dysuria, *i.e.* the more the patient strains, the more he passes, site of obstruction, and rectal examination will differentiate these from the prostate enlarged with age. The enlarged prostate may be associated with stricture urethra, as in case 2. Bladder neck obstruction and vesical growth may be differentiated by cystoscopy. Examination of nervous system will be helpful to exclude tabes dorsalis or disseminated sclerosis. X-ray will rule out calculus. Examination of the epididymis or complete renal or urinary examination may be helpful to exclude tuberculosis of prostate. Malignant prostate is usually very hard, rectal mucosa may be fixed. Pain, both local and referred, may be a feature. There may be associated metastasis in the pelvic bones. There is rise of acid phosphatase in the blood.

Digestive disturbances of renal failure should not be mistaken for gastritis or cancer stomach. Frequency should not be labelled polyuria or diabetes insipidus.

Management.—The principle of management may be discussed under two heads: (1) Urgent group, coming with retention or hæmaturia. Hot bath, morphine $\frac{1}{4}$ and atropine 100 gr. should be tried first. If they fail, a catheter should be passed with sterile precautions after local anaesthesia (novocaine 4 per cent). After injection of 20 to 30 cc. novocaine solution, the urethra should be massaged and the anterior urethra compressed with a penile clamp or with a piece of gauze. One should wait 5 to 10 minutes before catheter is passed. The metal catheter should be warmed and gradually passed, remembering the curvature of the urethra. When the gum elastic or metal catheter fails, a surgeon should be called in or the patient should be transferred to a hospital. It is dangerous to empty the bladder completely, as death from shock, renal hæmorrhage or anuria may occur. After about 2 weeks radical prostatectomy may be undertaken.

(2) Chronic group coming with dysuria, urgency, frequency, etc. This is a serious condition. There also bladder should be emptied slowly for reasons as given above either through a water-tight suprapubic stab puncture or by attaching a tap at the end of the urethral catheter or adjusting a bulldog clip to the rubber tube leading to the urinary bottle.

After about 2 to 3 weeks prostatectomy may be undertaken.

Hæmaturia.—Rest, morphine, calcium, vitamin C and K and bladder wash with silver nitrate

(1 in 10,000) may stop the hæmorrhage. If the hæmorrhage is severe and persistent, patient should be sent forthwith to a hospital. Suprapubic cystostomy, removal of blood clots, silver nitrate irrigation, packing of the prostatic urethra or even prostatectomy is necessary. Blood transfusion should be given with caution, after grouping. For recurring hæmorrhage, x-ray treatment may be advised. If it still recurs, two stage prostatectomy is indicated.

Management of chronic cases.—If the case is an early one, judged clinically by rectal examination, cystoscopy and amount of residual urine, testoviron propionate 25 to 50 mg. 1 M. bi-weekly may be tried. He should be examined every three weeks to check the residual urine, renal efficiency and general condition.

When the patient should be advised prostatectomy.—Repeated attacks of retention of urine, repeated hæmorrhage from prostate, chronic cystitis with vesical calculus or diverticula, impaired renal efficiency, residual urine more than five ounces are the usual indications of prostatectomy.

Special investigation before operation.—(a) Estimation of renal functions, like estimation of blood urea, urea clearance test, excretion pyelography, chromocystoscopy (0.4 per cent of indigo-carmin injection intravenously). The dye should appear through the ureteric orifice (within 4 or 5 minutes) should be first done. Intravenous pyelography is a very useful procedure for the estimation of renal function.

(b) Complete examination of urine.

(c) Examination of the cardiovascular system. Recently electrocardiography is advocated in some clinics.

(d) Other routine examination, *e.g.* respiratory and gastro-intestinal system.

(e) Blood should be grouped before operation and suitable blood should be kept ready for transfusion.

Choice of method

The choice of method varies with the individual surgeon. It appears that majority prefer suprapubic prostatectomy either in one stage or in two stages. Some prefer Freyer's technique, others prefer Harris's method. Terence Millin recommends retropubic extra-vesical prostatectomy. The chief advantage of Millin's method is in direct access to the prostatic cavity and to deal effectively the bleeding points and short convalescence. The disadvantages of Freyer's method are hæmorrhage and long convalescence. The writer follows modified Freyer's technique either in one or two stages. Out of 12, in 7 cases one stage prostatectomy and in 5 cases two stage prostatectomy were done. In cases with high blood urea, with repeated hæmorrhage, with cardiovascular damage, with chronic retention and bad cystitis two stage prostatectomy is the method of choice.

Technique.—If two-stage method is decided, first incision is made a little high to facilitate removal of prostate in the second stage. After opening the bladder, the cavity is visualized for the intravesical projection of prostate and for diverticula or calculus, if there is any. If vesical calculus is present, it is removed.

When the cardiovascular and renal functions improve, the second stage is undertaken. The time interval is about three weeks in average cases. The original scar is excised along with the fistulous track. The incision is extended down to the symphysis pubis. The anterior bladder wall is dissected free, with the precaution that the peritoneal cavity is not opened. The bladder is re-opened. After rupturing the mucous membrane, the finger lays open the line of cleavage between the adenoma and the compressed prostatic tissue. The finger is moved round in a complete circle. The prostatic urethra is torn across in front of the adenoma. Adhesions near verumontanum or anterior commissure or near the apex may give rise to difficulty. The adenoma, when free, is removed from the bladder cavity.

After enucleation one retractor is inserted at the lower angle and two on each side to visualize the trigone and the prostatic cavity. The tags of mucous membrane and the posterior sector of the prostatic rim is excised under vision, taking care not to injure the ureteric orifices. It has been observed on several occasions that besides the prostatic adenoma there may be present some hypertrophied cervical trigonal glands, looking like small marbles. They also should be enucleated, otherwise they may lead to post-operative obstruction and persistent fistula. The prostatic rim is sutured by few mattress stitches, especially at 4 o'clock and 8 o'clock position. The cavity is irrigated with cold saline or silver nitrate solution. Cold water irrigation is preferred to a hot water one. If the oozing from prostate cavity persists, roll gauze is packed for a few minutes.

When the cavity is fairly dry gel-foam or oxyeel is introduced into prostate cavity. The bladder is sutured in two layers leaving a suprapubic tube and a drain at the cave of Retzius. The suprapubic tube is removed on the tenth day and a urethral catheter is introduced. A soft catheter may refuse to go. Simple dilatation by a bougie will help the passage of catheter. By the above technique the fistula usually closes within three weeks. Post-operative penicillin and sulfadiazine and fluid *ad lib* are administered as a routine measure. Early ambulation is also encouraged.

Conclusion

1. Prostatectomy is no longer a dreaded operation in India.

2. Enlarged prostate appears to be more common in Hindus than Mohammedans. Out

of 12 cases, 11 were Hindus and one was an Anglo-Indian.

3. Although frequency, dysuria, and urgency were early features, most of the cases did not lay importance on those early symptoms, 75 per cent of cases reported for retention of urine, either acute or chronic.

4. Modified Freyer's technique is followed by the author, modification is almost like that of Thomson-Walker. The author could not secure the help of special bladder retractor and illuminator. Ordinary medium-size retractors with a spot lamp served fairly well.

Out of 12 cases, two died. Case 9 probably died of cardiac failure. His B.P. fell quickly and pulse rate increased; but the patient was not restless, there was no increase or decrease in Hb and there was no severe external hæmorrhage. The question of electrocardiography is given due thought by American urologists. They say that so-called post-operation shock is probably due to cardiac deficiency, 71 per cent who died had had serious heart trouble.

Case 9 died from hæmorrhage. In this case hæmorrhage could not be controlled by gel-foam. Blood transfusion was not possible immediately for want of blood. Packing of the prostate cavity and immediate blood transfusion might have saved the case.

5. Incidence of morbidity, like infection, persistent fistula, is much diminished by penicillin and sulfa drugs and in wedge resection of the posterior sector after vesico-prostatic opening.

This paper was read in the South Calcutta Doctors' Club in 1948. Some addition and alteration have been made in preparing it for publication.

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SEROLOGICAL TECHNIQUE : IMMUNOTHERAPY (contd.)

IMMUNIZATION AGAINST VIRAL INFECTIONS By S. D. S. GREVAL

VIRUSES and rickettsiae are probably essentially different from other micro-organisms which become parasites. The latter borrow

nourishment from the host while the former borrow life itself. Some of them (probably all of them at some stage) are mere crystals otherwise.

In borrowing life they sink deep into the tissues, inside the cells and sometimes the nuclei of the cells. The immunity against them, consequently, must be a tissue immunity rather than a humeral one.

In the vaccination against smallpox the virus of vaccinia probably enters the blood stream and is distributed to all the tissues. *Living* virus thus may remain in the tissues, at several foci, and serve as antigen: hence lasting immunity. Immunization with *killed* virus is not so lasting.

Immunization against smallpox

Vaccine: 1. *Lymph*.—It is the ground up eruption of cowpox.

(Vacca = cow. Hence vaccinia and vaccination, and later material for immunizing actively against any infection, bacterial or viral. Smallpox and cowpox are caused by the same virus modified in different animals. Hence the protection in man against smallpox by vaccination.)

Shaved and scarified abdomen of a calf (including buffalo calf) or a sheep is sown with seed lymph obtained from another animal. The eruption when mature is scraped, ground into pulp with 50 per cent glycerol in distilled water and stored for a long time at -10°C . The glycerol reduces the number of bacteria initially present in the pulp to the limit allowed by the law. The pulp is also tested for the potency of the virus in the shaved abdomen of a rabbit, as is also required by the law.

The standardized lymph is now put up in containers of various sizes, usually small corked tubes (25–100 doses) and hermetically sealed capillary tubes (single doses), and again left in cold storage. The containers when required for issue are removed from storage and labelled. The date on the label is really the date of the issue although it is called the 'date of manufacture'.

The user must use the lymph within one week of 'manufacture'. If he has a refrigerator to keep it in he can prolong its life by another week. Beyond that period he must not go.

2. *Vaccines obtained from virus cultivated in tissue culture, including plasma-clot-culture*.—They are free from bacteria.

3. *Vaccines obtained from virus cultivated on chorio-allantoic membranes of developing chick embryos*.—They are also free from bacteria.

The last two vaccines are not in common use. There is no reason why they should not be. Some of them can be freeze-dried without loss of potency and should be particularly useful in the tropics. Three types are available:

- (1) Freeze-dried tissue-culture virus of Rivers.
- (2) Glycerolated egg-culture virus of Good-pasture.
- (3) Freeze-dried plasma-clot-culture of Plotz.

Site and its preparation.—The usual site is the lower part of the posterior border of the deltoid muscle of the left side. The skin is cleaned with soap and water, and then rubbed with ether or spirit which is allowed to evaporate. Soap and water only will do. Ether or spirit only will do also. American workers swab the skin with acetone, gently, with or without a previous cleaning with spirit.

Leg has no advantage over the arm. In fact, it has a disadvantage inasmuch as the local and general reactions are more severe.

Technique: 1. *Cross-hatched scratches*.—They are no longer in vogue. The area and immunity relation does not hold.

2. *Simple scratch*.—A drop of lymph is deposited on the skin and a single scratch (preferably with Hagedorn needle) $\frac{1}{4}$ inch long made through it. Blood is not drawn. After the Glasgow epidemic (1942) the local public health authorities advocated 3 such parallel scratches. They may be well spaced, at least $\frac{1}{2}$ inch apart. The skin is held taut for making a scratch.

3. *Multiple pressures*.—This is the technique of choice now. A drop of lymph is deposited and 'pressures' are applied to the skin through the drop with the point of a Hagedorn needle held almost parallel with the surface. The needle is moved up and down, more to test the resilience of the skin (held taut) than to prick it, to apply:

30 pressures for primary vaccination of babies.

30 pressures for secondary vaccination of adults.

6–10 pressures for primary vaccination of adults. In view of the danger (*vide infra*) unvaccinated children may be classed with adults for primary vaccination.

The area pressed need not exceed $\frac{1}{8}$ inch in diameter.

The excess of lymph is removed gently from the area with a swab.

Pain of vaccination, risk of septic infection, pain of reaction and size of the scar are reduced.

4. *Intradermal injection*.—This can only be done with a vaccine cultivated on tissue or on chorio-allantoic membrane. Information on its efficacy is not yet available.

Reading of results.—The arm is examined at least twice: after 3 and 9 days. Ideally it is examined thrice: after 3, 7 and 9 days.

Four types of reaction are recognized :—

- (1) The well-known primary 'take'. The maximum diameter of redness reached in over 7 days. Scab off in 21 days.
- (2) The vaccinoid or accelerated reaction associated with re-vaccination and partial immunity. The maximum diameter of redness reached in under 7 days. Scab off in 8 days.
- (3) The immune or immediate reaction. The maximum diameter of redness reached in under 3 days. Papule only. No pustule or scab.
- (4) A weal-like reaction in some subjects in a few minutes. It has no significance in vaccination. The subjects are probably allergic.
- (5) No reaction.

Use of dressing, etc.—No dressing should be applied. The area should be exposed to the air : otherwise, aerobic bacilli, including *Clostridium tetani* which cannot be excluded from the lymph, might begin to grow.

The area is not wetted until a firm scab has formed.

Excessive oozing from the area may be stopped by swabbing its surface with cotton-wool dipped in absolute alcohol. The swabbing may be repeated.

A sterilized dressing may be worn on the inside of the sleeve against the area.

Age and seasons, etc.—Babies approaching 6 months in age react best. Younger babies may be refractory. Summer months are to be avoided, if possible, and the age reduced to 3 months if necessary. Nearly all encephalitis cases occur in summer in America. Besides, the lymph deteriorates more often in summer months. Primary vaccine at 6 months, secondary at 5 years and re-vaccination every 5 years constitute an ideal plan. A re-vaccination, however, is advisable whenever there is a local outbreak of smallpox or one passes through countries where smallpox usually occurs. Medical, nursing and sanitary staff likely to deal with smallpox should be vaccinated yearly.

Complications.—Apart from sepsis which is preventable by attention to the manufacture and to the technique there is a risk of post-vaccinial encephalitis. It operates only when the primary vaccination is done later than in infancy. As stated before the disease occurs in summer months. It follows the height of the vaccination reaction in 10 to 14 days and is often fatal. Improvement, however, is always rapid unlike what occurs in other forms of encephalitis, although residual mental retardation and spasticity may remain.

Tetanus may develop and need the specific treatment.

Generalized vaccinia may occur in subjects suffering from chronic skin disease or debility. It may be serious.

Opinion on the lymph from results.—A lymph giving many takes in primary vaccinations is satisfactory. A lymph giving many vaccinoid reactions in secondary vaccinations is also satisfactory. A lymph giving many immune reactions in secondary vaccinations may or may not be satisfactory. These reactions are given by the proteins in the lymph.

When a primary vaccination fails the presumption is that the lymph is faulty. The subject should be vaccinated again.

Contra-indications.—(i) Premature and malnourished babies, (ii) babies suffering or convalescing from acute infections, or during the incubation period (suspected from exposure) of such infections other than smallpox, and (iii) babies suffering from a skin disease should not be vaccinated. If possible other preventive inoculations, like anti-typhoid and anti-typhus, should be avoided at the time of primary vaccination. Anti-yellow fever inoculation should be avoided for 2 weeks before or 3 weeks after a primary vaccination.

Sufferers from chronic skin disease can only be vaccinated intradermally with bacteriologically sterile virus.

Premature and malnourished babies should be vaccinated when the weight for age is satisfactory or is rising satisfactorily.

These contra-indications are based on two reasons : (1) A baby below par in health may not be able to stand a severe reaction which might occur. (2) As the virus borrows life only from a healthy body, the vaccination may fail in a baby below par in health.

An incidental serological change.—Biologic false positive reactions for syphilis are known to occur after vaccination for as long as 4 months.

A Mirror of Hospital Practice

PULMONARY AMOEBIASIS

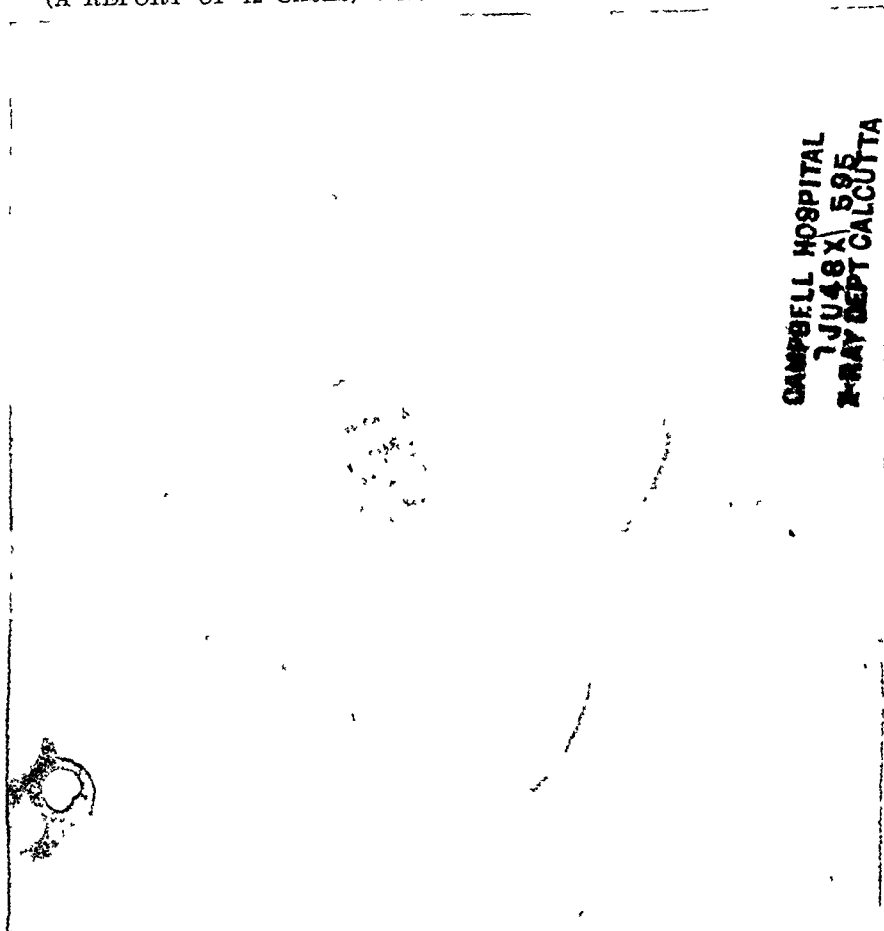
By S. K. MUKHERJEE, M.B. (Cal.), M.R.C.P. (Lond.),
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College Hospitals, Calcutta

AMOEBIASIS is protean in its manifestations but its pulmonary features are being detected only recently.

PLATE XX

ENLARGED PROSTATE, CLINICAL FEATURES, DIAGNOSIS AND MANAGEMENT
(A REPORT OF 12 CASES) : ASITA LAL SOM. (O. A.) PAGE 244



CAMPBELL HOSPITAL
7 JU 48 X 595
X-RAY DEPT CALCUTTA

PULMONARY AMOEBIASIS : S. K MUKHERJEE (M. H. P.) PAGE 250



Clinically, these may be classified into the following types : (1) Symptomatic, (2) secondary and (3) primary.

(1) *Symptomatic pulmonary amœbiasis*.—Its clinical features are quite common. Patients are seen complaining of fever and pain in the lower part of the right side of the chest. On examination, liver is found enlarged and tender while auscultation of the chest reveals pleural rub. Both hepatitis and pleurisy disappear on emetine therapy. There is another form in which amœbic liver abscess and amœbic hepatitis with upward enlargement of the liver are associated with signs of right basal involvement, characterized by feeble breath sounds and impaired percussion note. Skiagram does not show any pulmonary lesion except that the diaphragm is less mobile and situated abnormally high, whereas in certain other cases it reveals obliteration of the right costo-phrenic angle, suggesting pleural effusion. Following effective anti-amœbic treatment, signs in the chest disappear.

(2) *Secondary pulmonary amœbiasis*.—This is more common although its incidence is becoming less due to earlier recognition and effective therapy of amœbic hepatitis with or without formation of abscess. It is due to extension from the liver into the lung substance and pleuræ. This contiguous spread leads to necrosis of the lungs or empyema or both. The clinical picture is fairly well defined. The course of hepatic abscess is suddenly modified by empyema or pulmonary abscess. The latter event is characterized by expectoration of thick reddish pus, and rapid recovery follows if emetine is given at once. Empyema may develop without pulmonary involvement when hæmoptysis is absent. More commonly empyema and pulmonary affection co-exist (figure 2, plate XX). Emetine will not be enough to combat this type of empyema.

(3) *Primary pulmonary amœbiasis*.—This is rare and is probably due to embolism from the gut-wall. Clinically two types have been differentiated :

(a) *Amœbic pneumonitis*. Here the pulmonary reaction to amœbic invasion is not characterized by gross tissue destruction. Symptomatology of all the recorded cases is highly suggestive of pulmonary tuberculosis. Cough, hæmoptysis, loss of weight, night sweats and evening rise of temperature are the main symptoms while the pulmonary signs consist of impaired percussion note, weak breath sounds and a few crepitations on the right side of the chest, mainly at the base. X-ray of the chest

reveals an area of opacity highly suggestive of tuberculous infiltration. Repeated examinations of sputum for acid-fast bacilli prove to be negative. History of intestinal amœbiasis may or may not be available. A rapid clinical improvement with complete disappearance of the radiological opacity with emetine therapy is diagnostic.

Manson-Bahr (1931) reported such a case. More recently, Dormer and Friedlander (1941) reported seven cases, all responding to emetine therapy. Chaudhuri and Rai Chaudhuri (1946) described another two, both of which made rapid recovery after a course of emetine therapy.

(b) *Pulmonary amœbic necrosis*. Extensive destruction of pulmonary tissues simulating lung abscess characterizes this type. The main features are : irregular fever, cough, pain in the chest and tachycardia with signs of pneumonia rather than an abscess. Foul bloody expectoration soon becomes a feature of the disease. There is moderate leucocytosis. Skiagram of the chest reveals an opacity with a fluid level. Acid-fast bacilli are not detected in the sputum. Response to emetine is dramatic.

The following case is both interesting and illustrative.

Patient H. M., aged 35 years, was admitted into the writer's ward complaining of pain in the right side of the chest, cough with offensive expectoration, often sanguineous and irregular temperature for three months. He was emaciated and anæmic, his appetite poor and bowels irregular. Breath and expectoration were both offensive but no clubbing of the fingers was noted. Physical examination of the chest revealed diminished vocal fremitus, impaired percussion note, weak breath sounds and occasional râles in the lower interscapular and infrascapular regions on the right side. On further investigation, Hb. 40 per cent (Hellige); RBC 2,920,000 per c.mm.; WBC 8,300, poly 77 per cent, lymphocyte 22 per cent, monocyte nil, eosinophil 1 per cent; erythrocyte sedimentation rate 22 mm. 1st hour (Wintrobe corrected). Sputum was examined repeatedly for acid-fast bacilli with negative results. Skiagram showed an area of opacity with a fluid level (figure 1, plate XX). Provisional diagnosis of putrid lung abscess was made and penicillin 50,000 units 3-hourly was given parenterally. On the third day of penicillin therapy there was a good response but on the following day pyrexia increased. At this stage emetine therapy was instituted with remarkable effect. He became afebrile, halitosis disappeared, reddish purulent expectoration stopped and his appetite returned while physical examination of the chest showed

signs of cavitation, confirmed by skiagram. He was kept in the ward for a further period of two weeks when another skiagram (figure 2, plate XX) was taken which recorded progressive improvement.

This case shows that putrid lung abscess may be due to primary pulmonary amœbiasis. Response to emetine is diagnostic, though sputum should always be examined for *Entamoeba histolytica*.

Summary

1. Types of pulmonary amœbiasis have been classified.

2. Short clinical description of each variety has been described with the notes of a case of pulmonary necrosis due to *E. histolytica*.

My thanks are due to Dr. S. C. Sinha, Superintendent, for his permission to report this case.

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CHEMOTHERAPY IN HUMAN ANTHRAX

By P. C. DUTT, L.M.F.

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Case 1.—Alfos, an Oraon male labourer, aged 18 years, came to the hospital on 23rd February, 1948, with an inflammatory papule on his left cheek with surrounding induration and swelling. Duration about 24 hours; temperature 99.2°F.; pulse 94. He was given local treatment. On the next day his condition was found quite changed. The papule had turned into a blackish pustule and was surrounded by a ring of vesicles. The left side of his face was so swollen that the left eye could not be opened

due to œdema of the eyelids. The right side of the face was also markedly swollen. Temperature rose up to 104°F. and pulse to 120. A clinical diagnosis of cutaneous anthrax was made and confirmed by laboratory examination of a smear from the pustule which revealed anthrax bacilli. Blood film showed leucocytosis and no *BACILLUS ANTHRACIS*.

He was at once put on sulphapyridine 1 gm. four times daily and plenty of glucose alkaline drink. Locally, a dressing of sulphonamide in glycerine, 20 grains to an ounce, was applied. On 26th February, 1948, his condition showed definite improvement. Temperature came down to normal and the swelling was much reduced. Sulphapyridine 1 gm. was given three times and continued for three days more with 0.5 gm. doses three times daily. Sulphonamide ointment was then applied locally and the ulcer healed up within a fortnight.

Case 2.—Budhoo, an Oraon male labourer, aged 35 years, got a painful papular eruption on his right knee two days prior to his admission to the hospital on 10th March, 1948. On examination, a black pustule about the size of a rupee was found on his right knee-cap with surrounding induration and marked swelling. The right inguinal glands were enlarged and tender. Temperature 104.2°F.; pulse 124; and he looked toxæmic and very ill. Laboratory findings: Blood film and direct smear from the pustule both showed anthrax bacilli.

Treatment started with penicillin 100,000 units intramuscularly in five divided doses at 3 hours' interval and repeated on the next day. On 12th March, 1948, the temperature came down to normal with clinical improvement and also reduction of the swelling. He was then given five more injections of penicillin 10,000 units, each dose every three hours. The total amount of penicillin given in 3 days was 250,000 units. Local treatment consisted of dressings with sulphonamide in glycerine till separation of the black slough. Subsequently a soothing ointment containing sulphonamide and cod-liver oil in paraffin base was applied. The patient made an uneventful recovery.

Conclusion.—Two cases of cutaneous human anthrax, one treated with sulphapyridine and the other with penicillin, have been described. The results in both the cases were found prompt and successful.

My thanks are due to Dr. M. Warner, M.R.C.S., L.R.C.P., for his valuable advice and for permission to publish these notes. Thanks are also due to Dr. B. K. Chanda, L.M.F., L.T.M., Central Laboratory, Namrup, for his help in examining the smears.

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Indian Medical Gazette

JUNE

PLEASANT HOT WEATHER IN CALCUTTA IN 1949

As we observed in our April issue the season following the official cold weather in Calcutta was far from oppressive. According to the daily press a pleasant hot weather of this type had not been experienced for 15 years. We are indebted to the Director, Regional Meteorological Centre, Calcutta, for the accompanying tables of comparative figures of temperature, relative humidity and rainfall for March and April of this year and the corresponding months of the last year. Certain differences are striking indeed.

During the interval between the end of the cold weather (end of March) and the beginning of the monsoon (usually in July) life in Calcutta is made tolerable by nor'westers and nor'westers alone. Usually about 16 pass through Calcutta during this period. This year no less than 33 have done so up to the date of writing (30th June, 1949), 25 of them before the first shower of an early monsoon on 9th June.

With the commencement of the monsoon the nor'westers stop. When the monsoon fails or is arrested temporarily they start again: that is how the last five or six have come again.

A nor'wester is an occurrence familiar in Calcutta in particular and in Bengal in general.

The storms usually commence to form in the afternoon at about two or three o'clock, and often take place when the sky has small compact "woolpack" clouds, moving in from the south-east. Very often in April and May they commence for several consecutive days at about the same place at about the same time. In the districts of Dacca, Faridpur and Pabna, where they appear to be most frequent, they occur in April and May, from once every few days to once every week or so. The wind is often of great violence. Hailstones of over three inches in diameter are not unusual. I have seen two hundred cattle killed by hail in a single storm. These large hailstones may be sometimes seen falling few and far apart, when they . . . look like small white birds swooping down. Sometimes they occur mixed with rain and of many sizes.

The process of the formation of these storms is very interesting. One or two of the "woolpack" clouds before mentioned may be seen to tower in thin columns. These grow upwards and outwards and coalesce, forming large, heavy clouds round a central boiling mass

ascending rapidly to a great elevation. When at their height, the centre of the uppermost cloud flattens out in a circular white top, at first often iridescent. It rapidly extends to a great diameter. Directly the flat top begins to form there is a white precipitation, probably snow or hail. As soon as this commences, the whole mass of cloud beneath begins to move against the south-east ground wind, along with which it had, until this movement almost, been travelling. The storm may now be but small, or it may cover several square miles. I fancy this depends on the amount of moisture present in the ground current. As soon as the storm begins to move, generally in a south-easterly direction, the wind rises and lightning and thunder commence. Along the southerly rim a low rolling brow of cloud forms, turning upwards and outwards on itself, and from behind this comes the turmoil. The storm progresses until it blows itself out, generally about midnight, but occasionally not until daylight or later' (Sohoni, 1931).

The nor'wester, properly, is the storm without the thunder. Popularly, it also includes thunder, lightning, rain and hail. The consequent fall in temperature is remarkable.

Our interest in the pleasant hot weather in Calcutta is its possible unpleasant association with rats, fleas and *Pasteurella pestis*. We wonder if the years of the first outbreak of plague in Calcutta, 1897 to 1925 (Editorial, 1948), were also the years of pleasant hot weathers. We hope to ascertain and present to readers, later, this fact, from records which at present are not available.

Within living memory are treasured the not too remote pleasant hot weathers of Calcutta. 'The roads then were not tarred' is the usual explanation given by most mature residents.

Going further back, Macaulay, when he was writing the Indian Penal Code in Calcutta, in 1836, did not find the 'absurdly maligned' climate unpleasant at all (Trevelyan, 1889). He had then resided in Calcutta for nearly 2 years. His contemporaries and compatriots used to dine at one another's houses throughout the year and eat dinners of 12 courses or more. It must have been the pleasant weather which made possible the ingestion of the aforesaid rather large volume of food in the early days of the East India Company.

(Whether the ingestion really benefited the ingestors cannot be stated with certainty. A well-known writer on Calcutta is about to produce a book giving an account of the old cemeteries of the town and of 'The Britons who will not quit'. The average age of interment in those days was decidedly on the low side. These 'Haves' of the day ate and drank too well, finished their ration assigned by physiological laws and limits of the human system, and departed earlier than the 'Have Nots' here or in the country of their origin.)

TABLE I
Alipore (Calcutta)

March	TEMPERATURE (IN °F.)									
	Maximum		Minimum		At 0800 I.S.T.	At 0830 I.S.T.	At 1230 I.S.T.		At 1700 I.S.T.	At 1730 I.S.T.
	1948	1949	1948	1949	1948	1949	1948	1949	1948	1949
1	88.9	87.3	63.0	59.8	65.8	70.5	87.0	88.4	83.0	84.0
2	89.0	89.9	61.3	62.3	66.7	69.8	88.0	89.0	85.0	85.2
3	89.0	92.0	65.0	69.0	71.1	74.1	89.0	90.4	86.8	86.0
4	92.0	92.6	62.3	71.0	70.1	79.0	91.7	90.2	87.0	83.0
5	93.3	91.4	66.5	71.2	72.0	80.4	88.8	92.0	86.0	83.9
6	91.8	93.7	66.9	66.6	73.0	78.8	88.0	91.7	84.1	88.0
7	89.8	93.7	71.3	75.2	76.1	80.0	89.9	92.1	87.0	89.0
8	91.9	94.7	73.0	71.0	76.9	76.8	93.2	89.5	88.0	83.0
9	95.1	90.4	75.3	68.0	77.9	79.0	94.0	93.6	91.0	90.7
10	95.0	94.8	73.0	74.2	77.7	77.1	97.0	92.2	94.0	90.2
11	98.9	94.8	73.4	70.4	78.1	80.0	97.0	96.0	95.0	89.0
12	99.9	96.4	74.6	72.9	81.0	82.0	96.8	96.0	94.0	91.0
13	99.8	97.6	73.3	70.0	76.4	86.0	92.8	96.0	90.0	92.0
14	94.6	97.2	70.2	70.1	73.0	83.1	85.0	95.0	68.0	91.1
15	88.1	95.7	62.6	71.8	63.8	85.0	75.3	92.7	75.0	90.3
16	78.2	95.1	62.2	70.1	69.9	80.7	82.0	92.0	78.3	88.0
17	82.8	94.3	58.4	66.2	65.0	81.0	84.8	92.0	78.3	88.0
18	85.5	94.3	57.0	73.1	65.0	83.0	87.1	92.0	83.0	84.0
19	88.3	92.3	65.4	65.6	76.1	77.1	88.0	87.0	84.8	83.0
20	88.1	87.8	73.7	74.0	79.0	81.4	92.0	86.5	90.0	82.5
21	93.9	88.7	75.7	75.5	79.0	81.5	93.0	92.0	89.7	90.0
22	94.0	94.0	66.8	77.0	70.8	83.0	94.1	92.1	89.0	87.0
23	96.0	92.7	71.7	76.0	77.0	83.0	95.0	91.0	89.1	93.0
24	95.7	96.3	74.0	75.8	79.0	85.5	89.2	96.8	89.0	91.0
25	91.6	98.5	74.0	75.4	78.7	87.0	91.0	98.0	85.0	93.2
26	93.5	99.2	68.5	73.7	75.0	84.5	92.1	97.1	89.0	90.9
27	93.8	97.7	74.5	72.5	79.0	84.0	91.0	98.1	89.0	91.9
28	93.2	98.5	74.4	74.6	79.0	83.5	95.0	97.3	90.5	92.0
29	96.0	98.4	74.0	75.5	79.0	84.0	96.0	96.1	88.7	89.0
30	96.5	96.3	69.0	75.6	78.0	84.0	89.0	93.1	88.3	87.9
31	91.8	93.6	73.7	77.2	79.0	84.2	94.0	91.0	91.8	86.0

EDITORIAL

JUNE, 1949]

TABLE II
Alipore (Calcutta)

March	RELATIVE HUMIDITY (IN PER CENT)						RAINFALL (IN INCHES)	
	At 0800 I.S.T.	At 0830 I.S.T.	At 1230 I.S.T.		At 1700 I.S.T.	At 1730 I.S.T.	At 0800 I.S.T.	At 0830 I.S.T.
	1948	1949	1948	1949	1948	1949	1948	1949
1	64	69	21	23	27	27	0.00	0.00
2	91	82	21	22	24	32	0.00	0.00
3	53	83	30	29	31	39	0.00	0.00
4	55	80	26	46	37	67	0.00	0.00
5	83	72	44	40	21	53	0.00	0.00
6	85	60	46	33	34	40	0.00	0.00
7	93	68	47	29	40	45	0.00	0.00
8	91	51	40	27	40	46	0.00	t
9	91	58	41	32	48	31	0.00	0.00
10	83	84	28	26	31	33	0.00	0.00
11	86	59	26	24	30	27	0.00	0.00
12	41	67	23	23	29	31	0.00	0.00
13	73	39	41	19	44	28	0.02	0.00
14	84	40	53	24	97	30	1.51	0.00
15	86	39	64	19	68	25	2.70	0.00
16	59	30	29	13	25	21	0.24	0.00
17	65	67	23	32	26	34	0.00	0.00
18	76	72	20	45	30	64	0.00	0.00
19	79	65	49	60	61	69	0.00	1.28
20	82	76	48	63	50	73	0.00	0.00
21	74	76	27	51	29	33	0.00	0.00
22	71	75	17	54	24	65	0.00	0.00
23	93	75	22	35	30	35	0.00	0.00
24	58	66	44	33	51	34	0.00	0.00
25	58	46	39	26	35	33	0.00	0.00
26	63	37	39	19	49	24	0.00	0.00
27	87	68	54	22	47	31	0.00	0.00
28	87	73	42	26	48	36	0.00	0.00
29	87	71	43	25	64	41	0.00	0.00
30	79	71	56	55	57	65	0.35	0.00
31	90	60	44	49	47	65	0.00	0.00

TABLE III
Alipore (Calcutta)

April	TEMPERATURE (IN °F.)									
	Maximum		Minimum		At 0800 I.S.T.	At 0830 I.S.T.	At 1230 I.S.T.		At 1700 I.S.T.	At 1730 I.S.T.
	1948	1949	1948	1949	1948	1949	1948	1949	1948	1949
1	95.6	94.4	74.3	75.1	79.0	83.0	94.8	91.9	92.0	84.5
2	96.3	91.9	74.9	77.0	79.2	84.0	95.6	92.0	90.8	86.0
3	98.0	92.0	75.3	77.1	80.3	84.1	96.0	95.5	89.1	88.3
4	96.1	96.3	75.9	78.0	81.1	83.1	93.9	91.8	88.0	87.4
5	94.9	93.5	77.9	74.9	81.9	82.5	94.0	92.0	90.0	85.0
6	94.6	92.3	78.0	72.0	81.8	81.0	94.7	92.1	88.0	86.2
7	94.8	92.2	74.8	77.7	79.0	86.0	93.0	92.6	91.0	88.1
8	96.1	93.5	77.6	68.3	80.1	76.0	96.5	86.0	92.0	85.0
9	98.6	88.6	76.9	70.7	81.0	80.9	95.3	90.0	89.2	77.0
10	95.7	92.3	78.1	74.0	81.7	84.0	95.6	90.1	92.0	88.9
11	96.2	92.0	78.0	73.9	81.0	83.3	97.1	91.1	93.0	87.0
12	98.0	92.0	78.2	71.0	82.3	79.0	96.0	88.2	91.0	86.0
13	96.3	90.5	80.1	78.0	85.0	84.0	96.5	91.0	91.2	87.0
14	98.2	92.0	80.9	72.0	85.0	83.0	96.2	74.0	89.5	82.9
15	96.7	89.6	81.0	75.7	84.0	84.2	96.0	92.8	90.0	87.8
16	96.0	93.9	80.3	80.0	84.2	86.0	94.0	93.7	89.3	90.0
17	94.9	95.9	74.0	81.1	83.2	86.6	95.6	94.0	90.0	87.0
18	95.8	94.7	79.3	81.0	84.5	86.5	92.4	93.0	86.5	88.9
19	93.5	93.3	75.7	78.0	84.0	86.2	90.8	92.0	88.2	87.1
20	92.1	92.0	73.9	82.6	83.0	86.4	92.0	91.0	88.0	87.1
21	94.2	92.3	81.2	79.4	85.2	86.9	93.8	81.0	89.6	79.5
22	94.3	87.4	80.1	69.0	84.2	72.1	95.5	82.0	89.5	80.0
23	96.5	83.8	80.9	71.0	85.9	78.8	93.6	87.1	89.0	87.0
24	91.7	90.0	74.6	74.4	82.0	84.1	91.0	91.5	90.0	86.0
25	91.2	91.9	80.3	73.0	86.0	86.0	91.0	91.2	88.4	86.7
26	91.9	91.9	70.9	76.0	79.0	85.0	90.0	88.1	90.0	74.0
27	92.6	89.0	76.6	85.2	82.4	86.0	92.0	89.0	89.6	84.9
28	93.0	89.0	79.0	81.6	81.1	85.9	93.0	90.7	89.8	87.5
29	93.0	91.4	80.2	80.8	81.0	86.0	90.0	90.1	87.2	87.0
30	90.8	91.6	74.8	80.0	83.6	85.5	91.4	93.0	88.1	87.0

TABLE IV
Alipore (Calcutta)

April	RELATIVE HUMIDITY (IN PER CENT)						RAINFALL (IN INCHES)	
	At 0800 I.S.T.	At 0830 I.S.T.	At 1230 I.S.T.		At 1700 I.S.T.	At 1730 I.S.T.	At 0800 I.S.T.	At 0830 I.S.T.
	1948	1949	1948	1949	1948	1949	1948	1949
1	89	73	38	54	44	70	0.00	0.00
2	84	75	31	57	37	67	0.00	0.00
3	62	75	36	41	47	62	0.00	0.00
4	63	79	52	51	67	60	0.00	0.00
5	83	81	56	51	67	70	0.00	0.00
6	87	70	59	48	67	65	0.00	0.09
7	84	68	53	59	57	65	0.00	0.00
8	78	73	39	58	57	63	0.00	0.53
9	87	72	52	54	66	86	0.00	0.08
10	85	71	57	50	59	50	0.00	0.09
11	90	71	51	45	61	51	0.00	0.00
12	89	76	61	59	65	65	0.00	0.19
13	79	79	48	60	60	60	0.00	0.00
14	77	65	49	90	66	71	0.00	0.24
15	79	79	56	58	65	71	0.00	1.10
16	75	72	63	61	66	70	0.00	0.00
17	78	71	48	61	63	72	0.03	0.00
18	81	74	59	61	73	71	0.00	0.00
19	79	74	60	59	65	71	0.01	0.00
20	87	72	64	65	69	72	0.03	0.00
21	78	69	60	61	68	70	0.00	0.00
22	81	80	53	63	67	66	0.00	1.76
23	78	68	61	52	72	54	0.00	0.00
24	71	75	51	54	54	63	0.00	0.00
25	76	76	61	56	71	66	0.00	0.44
26	82	79	57	65	57	95	0.63	0.10
27	83	76	57	73	61	78	0.00	1.38
28	79	76	58	71	63	78	0.00	0.00
29	75	76	67	72	69	80	0.00	0.00
30	79	81	65	59	69	76	0.03	0.00

The weather during the arrest of the monsoon, in the third week of June, became oppressive suddenly and on 20th June accounted for the death from heat exhaustion of a well-known educationist in a famous school in Calcutta.

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ERRATUM

PNEUMONIC PLAGUE IN EASTERN INDIA

IN the above editorial published in the *I.M.G.*, **84**, April 1949, p. 157, column 2, para 5, line 34, for '1896' read '1897'.

Special Article

DIAGNOSTIC FLUOROSCOPY AND ITS POSITION IN TUBERCULOSIS CASE-FINDING

(A SUMMARY OF PREVAILING VIEWS)

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THE use of the fluoroscopy screen as a method of detecting pathological conditions in the chest is not new. In the early days of radiography it was the method of necessity, owing to low-powered equipment and the consequent long exposure time required to produce a good diagnostic film.

But with the advent of modern high power units, and ultra-fast x-ray film, fluoroscopy was relegated to a subordinate position. The absence of a permanent record following fluoroscopy was a serious drawback, but the development of the photo-fluorographic unit, and the use of miniature film, were further reasons for its subjection.

Within the past decade, however, there has been a revival of interest, in what is, undoubtedly, the cheapest and quickest form of diagnosis of pulmonary tuberculosis. The purpose of this note is to present an analysis of some of the available information on diagnostic

fluoroscopy, and to determine its value in modern case-finding methods.

In a recent article, Tattersall (1948) indicated that for two years (1946 to 1948) diagnostic fluoroscopy comprised the main feature of mass examination of suspected individuals at the Central Tuberculosis Clinic, Reading, England.

Of 2,908 patients sent for x-ray examination (fluoroscopy), 2,594 (98.6 per cent) were immediately discharged as 'normal'. At the end of 1948, no patient passed as 'normal' during the period under review, was subsequently found to have tuberculosis. The remaining 314 patients each had large film (14 × 17) examination, and eighty-five (26 per cent) were found to have pulmonary tuberculosis. Hence, of 2,908 suspected patients examined by fluoroscopy, 3 per cent were confirmed by later examination, nearly 90 per cent discharged as 'normal', and 7 per cent were referred back for further examination.

The method is recommended as being substantially cheaper and quicker than ordinary radiography. The average rate of working at the Reading Clinic is forty patients per hour. Neither film, processing equipment, highly trained technical staff, nor heavy expensive apparatus is required. One very great advantage is that the radiological report is available in a few minutes. Tattersall points out that *thorough* dark-adaptation is essential for accurate and consistent results.

One of the most enthusiastic and optimistic protagonists of fluoroscopy (Stiehm, 1941, 1942) contends that in the hands of an expert, and with suitable apparatus, this method of case-finding has definite advantages over radiography. He stresses that with fluoroscopy it is possible to examine the lungs from all positions, limits of inspiration and expiration can readily be seen; any small lesion detected in *any part* of the lung fields can be permanently recorded by means of a 'spot-film' (6 × 8), thus saving the cost of a large film. Only low-powered apparatus is required (80 K.v., 30 m.A.), and the method is available in any x-ray department fitted with a fluorescent screen.

It is a matter of interest to note that this investigator constructed his own type of apparatus, including a 'spot-film' device, which now forms an essential part of the majority of modern x-ray units.

Stiehm also evolved a very complicated 'fluoroscopic formula' by which the patient was examined in a large number of positions. He recommends that at least twenty minutes be spent in a darkened room before attempting the first fluoroscopic examination.

Recognizing that an x-ray examination is not an end in itself, for determining tuberculosis, the same author suggests that tuberculin testing should take place at the same time that radiological investigation is being carried out.

Two investigators, Chadwick and Pope (1946), after reviewing many hundreds of x-ray examinations, are satisfied that 'x-ray examination by fluoroscopy will demonstrate an infiltration in the lungs before characteristic symptoms appear, and thus long before signs of the disease can be clinically detected'.

These investigators are of the opinion that fluoroscopy 'presents the observer with a living picture of the individual', and that accurate diagnosis is limited only by the experience of the operator.

Having considered the substitution of fluoroscopy for radiography, they agree that, from the standpoint of cost, advantage lies with fluoroscopy. It is possible to examine from twenty to thirty patients an hour at a negligible cost.

Both Blatt and Greengard (1946) are agreed that fluoroscopy is the best form of examination in the diagnosis of tracheo-bronchial tuberculosis in children, since the child may be turned in various positions, and glands in the retro-cardiac space (which normally should be clear) may be readily visualized. A small film should be taken of any suspicious area.

After a large number of examinations, Heaf and Rusby (1948) are satisfied that fluoroscopy is the only method of obtaining a full survey of all lung areas. Special attention is given to the 'lordotic position'. In this view the patient, while undergoing fluoroscopy, holds the sides of the x-ray stand with both hands, and bends slowly backwards and forwards until the observer obtains the best view of the sharp triangular shadow of the lesion. When this is obtained, a small film of that area is taken.

Following upon the results of 800 fluoroscopic examinations, Fellows and Ordway (1928) were gratified to discover how small a lesion can be located by this method. They are of the opinion that fluoroscopy, for large groups, is rapid, economical and sufficiently accurate for all practical purposes, and express the hope that, 'with added experience, its application in preventive and industrial medicine will be demonstrated'.

Early in 1944, Bloch and Tucker started to fluoroscope all women attending the pre-natal clinic of Chicago Lying Hospital with very good results. The women were examined under the fluoroscope before proceeding to their particular clinic, and results of the radiological findings were entered upon their case records.

These two investigators are of the opinion that in a medical teaching school, recognition and appraisal of intrathoracic disease is of primary importance. Fluoroscopy is the only convenient method of instruction at the present time in many centres.

After fluoroscopic examination of 20,000 individuals, Bloch (Bloch, 1941; Bloch *et al.*, 1940)

considers that cost of this form of investigation is lower than tuberculin testing, and is a 'wholly satisfactory method of examination. It provides the advantage of looking at the living chest, of seeing, not only anatomical and pathological detail, but, to some extent also, physiological manifestations, such as the function of the diaphragm and cardiovascular system'.

Experienced personnel is essential, and Bloch considers that after fluoroscopic examination of sixty to seventy patients, eye fatigue is liable to interfere with accurate observations. He reaches the conclusion that fluoroscopic examination, carried out by experienced examiners and supplemented by x-ray films where necessary, is a reliable method of case-finding in tuberculosis.

Hall (1942) fluoroscoped 1,370 factory workers, mostly women, and found an incidence of 3.5 per thousand of significant tuberculous lesion. This figure closely approximates with that obtained with mass radiographic examination. This investigator is satisfied that, in skilled hands, fluoroscopy can attain a high degree of accuracy.

After fluoroscopic examination of many hundreds of patients for suspected tuberculosis, Israel and Hetherington (1941) concluded that an observer with even only moderate x-ray experience should be able to detect almost all lesions by this method. Failure to approximate the incidence obtained by photo-fluorographic methods is almost always due to lack of 'dark-adaptation'.

After analysing 973 cases, subjected to both fluoroscopy and diagnostic radiography, these investigators reported that, 'fluoroscopy should detect almost all tuberculosis infiltrations of clinical significance. In this series of nearly 1,000 examinations only in four cases were significant lesions not recognized'. These figures compare very favourably with those obtained by mass radiography.

Both investigators confirmed that variability of visual acuity of observers is an important factor in accurate diagnosis.

Stauffer (1945) fluoroscoped 1,038 civilian employees in an advanced naval base during the late war, and found the method a most useful, economical and accurate 'sieve'.

In contrast to the very convincing evidence supplied by a number of eminent investigators as to the value of diagnostic fluoroscopy, there are also many workers who consider that this method of tuberculosis case-finding is inaccurate and open to abuse.

Chalek and Bergh (1940) report that, after observing a large number of fluoroscopic examinations, they are of the opinion that with this form of investigation the observer is apt to give too much attention to insignificant conditions such as: small calcified foci, areas of

apical pleural thickening, hilar enlargement and cardiac distortion.

In their view, 'fluoroscopy is considerably less accurate than radiography'.

Discussing the economic advantages of diagnostic fluoroscopy, Garland (1942) reached the conclusion that, in the case of a private practitioner, this method, plus clinical examination, takes too much time.

Assuming that it takes ten minutes for clinical examination of the chest, twenty minutes for thorough 'dark-adaptation' and ten minutes for efficient fluoroscopy, the method is uneconomical. In hospital work, of course, there is normally a radiologist and clinician—the patient merely following on from the former to the latter.

This investigator is also of the opinion that the general public, medical and otherwise, places too much reliance upon the value of fluoroscopy. While admitting that fluoroscopy is simple and economical—providing the examiner is well 'dark-adapted' and knows how to interpret shadows on the fluorescent screen—the method has disadvantages.

The chief objection is that fluoroscopy does not permit detection of small infiltrates and cavities, and there is no permanent record for future reference. On the other hand, it is well known that clinically significant infiltrates may also be missed by radiography, especially when only one view is taken.

During the course of his experiments Garland estimated that the percentage of error of fluoroscopy (as compared with radiography) in the detection of tuberculosis varies from 13 per cent to 35 per cent—even in the hands of experts. He reaches the conclusion that: 'fluoroscopy is not sufficiently accurate to be relied upon for the detection of active tuberculosis lesions'. He however, agrees, that the method is more accurate than physical examination.

Studying 1,035 supposedly 'normal' individuals, Reid (1934), with fluoroscopy and diagnostic radiography, detected eight cases of pulmonary tuberculosis by the former method and ten by radiography. This investigator reaches the conclusion that the best means of detecting pulmonary tuberculosis is by use of stereo-films.

It is her opinion that fluoroscopy is approximately as accurate as photo-fluorography—or the taking of only ONE large film, in the anteroposterior position.

Comparing the results of 2,500 examinations made by fluoroscopy and radiography, Fellows and Ordway (1937) are of the opinion that 13 per cent of clinically significant tuberculosis lesions were missed by fluoroscopy.

Studying a similar number of cases (2,500), Voigtlander (1935) concluded that in 32 per cent of the fluorographic examinations the diag-

nosis was either incorrect or insufficient, whilst Schaare (1937) compared the results of 400 cases of suspected tuberculosis by fluoroscopy and radiography, and found an error of 18 per cent in the fluoroscopic findings.

Edwards (1940), after reviewing the mass surveys of over 100,000 individuals in New York, is of the opinion that any advantages credited to fluoroscopy are outweighed by its disadvantages, such as:

- (a) Accuracy of diagnosis is hampered by the human element;
- (b) Fluoroscopy represents the impression of a single individual;
- (c) Fluoroscopy has no permanent record that can be compared with subsequent examinations.

His report concludes: 'In mass surveys we have found the x-ray film to be more satisfactory, regardless of the extra cost involved'.

Examining 347 young adults by both fluoroscopy and stereo-radiography, Hetherington and Flahiff (1933) found the former method frequently failed to detect pulmonary infiltration, especially when limited to the apices. But in most instances it detected the more intensive lesions.

Further comparisons were made with 150 children (12 to 14 years) and it was found that, whereas fluoroscopic examination gave 'negative' diagnosis in every case, stereo-films (taken immediately after fluoroscopy) disclosed five cases of calcified lesions.

As a result of their investigations the authors are of the opinion that: '(a) . . . fluoroscopy fails to reveal a considerable part of the calcified nodules of lungs and lymph glands—although such calcifications are clearly visible on the large film, (b) . . . fluoroscopy seldom reveals any infiltration of the apices, (c) . . . x-ray films, taken in different positions, supply as much information as fluoroscopy and, in addition, show a wealth of detail not revealed by fluoroscopy'.

Physical factors of diagnostic fluoroscopy

The considered opinions of a number of eminent observers regarding the value of diagnostic fluoroscopy has been given. But certain investigators have also endeavoured to ascertain the reasons for such large discrepancies between different observers when viewing the same fluorographic image.

The great variation in diagnosis revealed by different observers during fluoroscopy is, suggests Pichard (1927), largely the result of properties of the human eye. X-ray films are always viewed in a bright light, whereas fluoroscopy is carried out in relative darkness.

As is well known, nerve impulses, initiated by light on the retina, are first received by the layer of rods and cones at the back of the eye, and then transmitted *via* nerve fibres to the brain.

For ordinary vision, in bright light, the whole retina (employing both rods and cones) is employed. But the fovea centralis, most sensitive part of the eye, contains cones *only* which are insensitive in dim light. For dark vision the visual purple (a photo-chemical substance only associated with the rods) is necessary.

From this it will be appreciated that when viewing x-ray films the whole retina is employed; but in a darkened room only the peripheral parts of the retina are employed. It has now been scientifically established that ability of an individual to see in the dark depends on many factors such as temperament, physiological condition and vitamin intake; further, this function can vary from day to day.

Under these conditions it is not surprising, therefore, to encounter considerable divergency as to what two observers actually 'see' when looking at faint shadows in a dim light.

Chamberlain (1942) in a number of carefully conducted experiments demonstrated that perceptive accuracy of the human eye is diminished as illumination is diminished. But this does not mean that *diagnostic* accuracy is impaired. Providing the observer can actually see faint shadows cast upon the fluorescent screen, any interpretation given to such shadows is the result of individual knowledge and experience.

The visual perfection in darkness of thirty physicians was tested by Chantraine and Cramer (1937). The test consisted of enumerating, from a fixed distance, lead numbers of various sizes mounted on a standard fluorescent screen. Six of the observers were classified as 'good'. Ten were 'medium' and fourteen could only be classified as 'poor'. Two-thirds of the observers needed more than ten minutes to acquire minimum 'dark-adaptation'.

The investigators recommend that visual acumen of individuals engaged in fluoroscopic diagnosis should be tested before engaging upon such work. With a knowledge of their 'dark-adaptability', observers would then have a pre-determined assessment of their capabilities in the diagnosis of faint shadows.

Licht (1936) made a series of careful photometric tests under various conditions of fluoroscopy. These tests showed that reduced illumination diminished the capacity of the eye to distinguish contrast and form.

Although detail was actually on the screen (as measured by the light meter), there came a point when faint shadows could not always be appreciated by the retina.

Licht concluded that if fluoroscopy is performed by a skilled observer, with good dark vision, it is an economical form of investigation. But films should be taken of all 'suspected' cases, and always of those individuals whose adiposity makes it impossible to obtain good visual illumination on the screen.

Discussion

The published reports of thirty-six investigators into the relative merits and demerits of diagnostic fluoroscopy are analysed above.

It is interesting to note that in the case of Hetherington there appears to be some modification of opinion. In 1933, in collaboration with Flahiff (1933), he reached the conclusion that, 'fluoroscopy fails to reveal a considerable part of the calcified nodules of lungs and lymph glands—although such calcifications are plainly visible on the x-ray film'.

However, in 1941, working with Israel and Hetherington (1941), he stated: 'An observer with even only moderate x-ray experience should be able to detect almost all lesions by this method, i.e. fluoroscopy'.

Technical improvements in radiographic equipment has also contributed largely to the success obtained by investigators within the last five years.

Examination of the published reports show that sixteen observers, after examining over 80,000 individuals, are of the opinion that diagnostic fluoroscopy is an accurate, cheap and speedy method of tuberculosis case-finding. On the other hand, thirteen observers, with over 100,000 examinations, have reached the conclusion that this form of investigation (although cheaper than radiography) is comparatively inaccurate. In addition, there is a lack of evidence for future reference.

Five investigators confined themselves to physical aspects of fluoroscopy, and indicated that individual physiological limitations might play a large part in respect of inaccurate diagnosis.

It is conceded that advocates on both sides have presented a strong case.

From his own experience the present writer is of the opinion that fluoroscopy has a definite value in tuberculosis case-finding—even its opponents appreciate rapidity and economy—but there remains the very definite disadvantage of lack of evidence.

As the result of his own work and investigations, the writer would like to place on record the following conclusions:

(a) It is universally recognized that both radiography and fluoroscopy have a definite value in tuberculosis case-finding.

(b) Photo-fluorography (mass radiography) should constitute the first 'sieve'. This presents permanent evidence for future consultation, if necessary.

(c) After interpretation of the miniature film, all 'suspected' cases should be fluoroscoped, and a 'spot-film' (6 × 8) taken of any possible lesion or suspicious area.

The advantages of this suggestion are:

(1) The presence of a radiologist is not required for the initial 'sifting'.

(2) In all 'suspected' cases the radiologist can carry out a thorough investigation of the lung fields.

(3) If any pathological condition is discovered, a 'spot-film' of that area can be taken.

(4) Only in exceptional cases need a large film (14 × 17) be taken.

(5) The method suggested combines permanent evidence (micro-film), with thoroughness of diagnostic fluoroscopy, plus economical use of large films.

Summary

A review of published literature from thirty-six observers is given covering nearly 200,000 radiographic and fluoroscopic examinations. The relative merits and demerits of diagnostic fluoroscopy are discussed.

An attempt is made to assess the value of fluoroscopy in tuberculosis case-finding, and the writer puts forward a suggestion for the incorporation of both photo-fluorography and fluoroscopy as an initial method of case-finding.

Where necessary a 'spot-film' is recommended of the suspected area, reserving the large film (14 × 17) for special examination.

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Medical News

INTERNATIONAL AND FOURTH AMERICAN CONGRESS ON OBSTETRICS AND GYNÆCOLOGY

14TH TO 19TH MAY, 1950, HOTEL STATLER, NEW YORK CITY

FURTHER plans for holding this international gathering have recently been announced by the sponsoring group, the American Committee on Maternal Welfare.

The preliminary programme for the scientific sessions, as developed by the General Programme Committee of which Dr. Howard C. Taylor, Jr., of New York is the Chairman, is as follows: The morning meetings, Monday through Friday, 15th to 19th May, will be general sessions each devoted to one of five topics: (1) physiology of human reproduction, (2) the pathology of human reproduction, (3) social and economic problems, (4) neoplastic diseases of the female reproductive system, and (5) obstetric and gynaecologic procedures.

The afternoons will be given over to meetings of various groups represented at the Congress, including nurses, nurse-midwives, hospital administrators, educators, practising physicians, investigators in special fields and public health doctors and nurses. Arrangements for these meetings are under the direction of the following committees, medical section, Dr. Newell W. Philpott, Montreal, Quebec; educators and investigators, Dr. George W. Corner, Baltimore, Maryland; hospital administrators, Dr. G. Otis Whitecotton, Oakland, California; public health, Dr. Edwin F. Daily, Washington, D.C.; and nurses and nurse-midwives, Miss Margaret A. Losty, R.N. of New York City.

The technical exhibit is under the direction of a special committee of which Dr. Woodard D. Beacham of New Orleans is chairman. Dr. John Parks of Washington, D.C., heads the committee in charge of the scientific exhibit. The committee in charge of arranging the motion picture programme is under the direction of Dr. Archibald D. Campbell of Montreal. Applications for space in the scientific exhibit or for time on the motion picture programme should be submitted to the chairmen in charge of these activities on official application blanks obtainable from the business office of the international congress at 24, West Ohio Street, Chicago 10, Illinois.

All inquiries pertaining to the meeting should be addressed to the Chairman of the International and Fourth American Congress on Obstetrics and Gynaecology, Dr. Fred. L. Adair, at 24, West Ohio Street, Chicago 10, Illinois. Mr. Karl S. Richardson is Business Manager. The site of the meeting, the Hotel Statler in New York City, was formerly the Hotel Pennsylvania.

10,000 LONDON CHILDREN TO BE X-RAYED

(From Release No. B.F. 899 issued by the British Information Services, Office of the U.K. High Commissioner in India)

MORE than 10,000 London children will be x-rayed by mass miniature radiography under a new health plan worked out by the local authorities. The plan has been given wide support by parents.

Health authorities believe that the majority of children in the East End will benefit from this free service when the x-ray apparatus becomes available in the summer.

The first experiment of mass x-ray in schools was made at West Ham. Letters sent to parents explained that should anything abnormal be discovered in the child they would at once be told and the school medical officer advised so that arrangements could be made for treatment.

RULES 64 OF THE DRUGS RULES, 1915

Appendix A

STABILITY AND STORAGE CONDITIONS OF DRUGS IN SCHEDULE C AND C(1) OF THE DRUGS RULES, 1915

Item No.	Preparations	Storage conditions	Stability
(I) Storage below 0°C.			
1	Vaccine lymph	Preferably below 0°C.; never above 5°C.	Kept at below 0°C.—6 months. Kept between 5° and 10°C.—2 weeks.
2	Yellow fever vaccine	(a) Preferably below 0°C. but never above 5°C. throughout dating period. (b) In nitrogen filled, hermetically sealed ampoules. (c) Product must be dispensed in unopened glass container in which it was placed by the manufacturer. (d) Protected from light	At 0°C.—3 months. At still lower temperature—longer.
(II) Storage between 0° and 10°C.			
1	Preparations of sera and antitoxins in liquid state.	(a) Stored between 2° and 10°C., preferably at lower limit. (b) Product must be dispensed in unopened glass container in which it was placed by the manufacturer.	5 per cent deterioration each year, if kept at 5°C., deterioration is greater at higher temperature. One year if the serum has 20 per cent excess over the declared potency. Two years if the serum has 30 per cent excess over the declared potency. Three years if the serum has 40 per cent excess over the declared potency. Four years if the serum has 50 per cent excess over the declared potency.
These standards cannot naturally apply to products like 'normal horse serum' and such other sera as cannot be evaluated in terms of International standard units. In such cases it shall be sufficient if the date of manufacture is indicated on the label.			
2	All vaccines and antigens except—(a) Vaccine lymph and (b) yellow fever vaccine.	(a) Stored between 2° and 10°C., preferably at lower limit. (b) Product must be dispensed in unopened glass container in which it was placed by the manufacturer. (c) Protected from light (d) Must not be allowed to freeze	<i>Typhus vaccine</i> —1 year (if kept at 4°C. in the dark). <i>Formolized anti-plague vaccine</i> —3 years (kept at below 4°C.). <i>Carbolized anti-rabic vaccine</i> —6 months (if kept in a cool place). <i>Antityphoid-paratyphoid (T.A.B.) vaccine</i> (the date of manufacture must be given on the label).
3	All toxins and toxoids except—(a) Undiluted old tuberculin, (b) diphtheria toxoid and (c) tetanus toxoid.	(a) Stored between 2° and 10°C., preferably at lower limit. (b) Product must be dispensed in unopened glass container in which it was placed by the manufacturer. (c) Must not be allowed to freeze	18 months. <i>Schick test toxin</i> —6 months.
4	Normal human serum	(a) Stored between 2° and 10°C. (b) Product must be dispensed in unopened glass container in which it was placed by the manufacturer. (c) Dried serum must not be exposed to excessive heat.	Liquid serum—6 months.
5	Human immune globulin.	(a) Stored between 2° and 10°C., preferably at lower limit. (b) Product must be dispensed in unopened glass container in which it was placed by the manufacturer.	

Appendix A—(contd.)

STABILITY AND STORAGE CONDITIONS OF DRUGS IN SCHEDULE C AND C(1) OF THE DRUGS RULES, 1945.—(contd.)

Item No.	Preparations	Storage conditions	Stability
6	Penicillin	(a) In hermetic container (b) Protected from action of moist air.	2 years. Crystalline penicillin is stable at ordinary temperature, if kept in sealed ampoules protected from action of moist air.
7	Injection of penicillin	Stored at below 4°C.	Kept below 4°C.—7 days.
8	Liquid extract of ergot	(a) Stored in as cool a place as possible. (b) In a completely filled container of small capacity (2 oz.). (c) Addition of ascorbic acid in suitable proportion (0.5 per cent).	1 year.
9	Citrated normal human plasma.	(a) Stored between 2° and 10°C. (b) Product must be dispensed in unopened glass container in which it was placed by the manufacturer. (c) Dried plasma should not be exposed to excessive heat. (III) Storage between 10° and 20°C.	6 months.
1	Preparation of sera and antitoxins in dry state.	(a) Stored at below 20°C. (b) Incomplete dry condition	Stable.
2	(a) Penicillin injection in oil and wax. (b) Penicillin tablets (c) Penicillin troches (d) Penicillin ointments	(a) Stored at below 15°C. (b) In hermetic or tight container or in collapsible tube (ointment) protected from moisture.	2 years.
3	Tetanus toxoid	(a) Stored at below 20°C. (b) Product must be dispensed in unopened glass container in which it was placed by the manufacturer.	2 years.
4	Pituitary (post. lobe) extract.	(a) Stored at below 20°C. (b) Must not be allowed to freeze (c) Reaction of the solution should lie between the limits of pH 3 and pH 4.	18 months. Retention of potency even up to 3 years is not uncommon; possibly addition of preservatives and other factors contribute towards better stability in special cases.
5	Insulin— (a) Insulin injection (b) Protamine-zinc insulin injection. (c) Globin insulin injection.	(a) Above 0°C. but not exceeding 15°C. (b) Must not be allowed to freeze (c) Dispensed in unopened multiple dose completely-filled container (capacity approximately 10 cc.) in which it was placed by the manufacturer. (d) Reaction of the injection should lie between the limits of pH 3 and pH 4.	2 years.
6	Arsenicals	<i>Neoarsphenamine and sulpharsphenamine</i> (a) Stored at below 20°C. (b) In hermetic containers of colourless glass from which air has been evacuated or replaced by an inert gas. (c) Sterilized prior to filling (d) Tryparsamide should be protected from light.	<i>Neoarsphenamine</i> —3 years. <i>Sulpharsphenamine</i> —5 years. Tryparsamide—5 years.
7	Gonadotrophic hormone	(a) Stored at below 20°C. (b) In a well-closed container in dry state.	1 year.

Appendix A—(contd.)

STABILITY AND STORAGE CONDITIONS OF DRUGS IN SCHEDULE C AND C(1) OF THE DRUGS RULES, 1945.—(contd.)

Item No.	Preparations	Storage conditions	Stability
8	Liver extract— (a) Liver injection (b) Dry extract of liver. (c) Liquid extract of liver.	<i>Injection :—</i> (a) Preferably not above 20°C. (b) In single dose hermetic containers. (c) Protected from light <i>Dry extract :—</i> (a) Preferably not above 20°C. (b) In hermetically sealed glass containers so as to exclude moisture. <i>Liquid extract :—</i> (a) Preferably not above 20°C. (b) In tight containers (c) Protected from light	
9	Ergonovine maleate injection.	(a) Stored at a temperature above 0°C. but not exceeding 12°C. (b) Protected from light	
10	Synthetic oleovitamin D.	Not exceeding 15°C.	
(IV) Storage between 20° and 30°C. (cool place)			
1	Protein hydrolysate and thromboplastin.	(a) Stored in a cool place (b) Protected from light	1 year.
2	Posterior pituitary powder.	(a) Not above 30°C. (b) In hermetically sealed container	Stable.
3	Dichlorophenarsine hydrochloride.	(a) Preferably not above 25°C. (b) In hermetic containers of colourless glass from which air has been evacuated or replaced by an inert gas. (c) Sterilized prior to filling	3 years
4	Oxophenarsine hydrochloride.	(a) Preferably not above 25°C. (b) In hermetic container	2½ years
5	Antimony preparations— (a) Stibophen (b) Urea stibamine	<i>Stibophen :—</i> (a) In hermetic container (b) Protected from light (c) Should not be brought in contact with iron or its compounds. <i>Urea stibamine :—</i> Stored in hermetically sealed containers from which air has been evacuated or replaced by an inert gas.	Stibophen—5 years. Urea stibamine—3 years
6	Adrenaline and solutions of salts of adrenaline— (a) Injection of adrenaline chloride. (b) Injection of adrenaline tartrate. (c) Strong injection of procaine and adrenaline. (d) Weak injection of procaine and adrenaline. (e) Adrenaline tablets (f) Procaine adrenaline tablets.	<i>Adrenaline solutions :—</i> (a) In well-filled and well-closed containers, preferably in single-dose sealed glass containers. (b) Protection from light <i>Adrenaline and procaine-adrenaline tablets :—</i> Protected from light	<i>Adrenaline in presence of procaine deteriorates much more rapidly. Weak solution is preferable, as in this adrenaline solution and procaine solution are mixed just before use.</i> <i>Adrenaline tablets—18 months.</i> <i>Adrenaline in procaine-adrenaline tablets—unstable as solutions.</i>
7	(a) Ergot (b) Prepared ergot	<i>Ergot :—</i> (a) Thoroughly dried (b) Kept entire <i>Prepared ergot :—</i> (a) In well-closed container (b) Stored in a dry place	Fairly stable. (Approximately—2½ years.)

Appendix A—(contd.)

STABILITY AND STORAGE CONDITIONS OF DRUGS IN SCHEDULE C AND C(1) OF THE DRUGS RULES, 1945.—(contd.)

Item No.	Preparations	Storage conditions	Stability
8	Vitaminized oil	(a) In well-filled, well-closed container. (b) Protected from light	Fairly stable.
9	Thyroid	In well-closed container	Fairly stable.
10	Any other preparation in a form to be administered parenterally— (a) Calciferol (b) Solution of calciferol. (c) Camphor (d) Ergotoxine ethanesulphonate. (e) Hyoscine hydrobromide. (f) Hydnocarpus oil (g) Ethyl esters of hydnocarpus oil. (h) Sodium morrhuate injection. (i) Parathyroid injection. (j) Suramin (k) Soluble thiopentone.	<i>Calciferol</i> :— (a) In hermetically sealed glass container, from which air has been evacuated or replaced by an inert gas. (b) Protected from light <i>Soluble thiopentone and ergotoxine ethanesulphonate</i> :— (a) In an atmosphere of nitrogen in sealed tubes. (b) Protected from light <i>All other preparations except camphor and parathyroid injections</i> :—Protected from light in well-closed containers. <i>Camphor and parathyroid injection</i> :—Do not need protection from light.	Fairly stable.
(V) Storage at ordinary temperature			
1	Toxins— (a) Diphtheria prophylactic toxoid, undiluted. (b) Old tuberculin, undiluted.	Product must be dispensed in unopened glass container in which it was placed by the manufacturer.	<i>Diphtheria toxoid</i> —2 years. <i>Old tuberculin</i> —stable.
2	Adrenaline	(a) Kept dry (b) In dark coloured sealed glass container (protected from light).	Stable.
3	Preparations of digitalis group of drugs not in a form to be administered parenterally— (a) Digitalis powder (b) Digitalis tablets (c) Tincture of digitalis. (d) Tincture of strophanthus.	<i>Digitalis powder</i> :— (a) Kept in air-tight container (b) Kept in light-resistant container. <i>Tablets</i> :— (a) Kept in well-closed container (b) Protected from excessive heat <i>Tinctures</i> :— (a) Kept in completely filled, well-closed container. (b) Avoid exposure to direct sun light or excessive heat.	<i>Digitalis powder</i> —stable. <i>Tablets</i> —less stable (2 years). <i>Tinctures</i> —less stable (2 years).
4	Injectable preparations of digitalis group— (a) Digitalin (b) Digoxin (c) Oubain (d) Strophanthin	<i>Digitalin and digoxin</i> :—In well-closed container, protected from excessive heat. <i>Oubain, strophanthin and digoxin injection</i> :— (a) In air-tight container (b) Protected from light	<i>Digitalin and strophanthin</i> —3 years. <i>Digoxin and oubain</i> —stable (at least 5 years).
5	Ergot alkaloids— (a) Ergometrine maleate. (b) Ergotamine tartrate.	(a) In sealed ampoules under nitrogen. (b) Protected from light	Fairly stable.

Appendix A—(concl'd.)

STABILITY AND STORAGE CONDITIONS OF DRUGS IN SCHEDULE C AND C(1) OF THE DRUGS RULES, 1945.—(concl'd.)

Item No.	Preparations	Storage conditions	Stability
6	Fish liver oils— (a) Cod liver oil (b) Halibut liver oil (c) Shark liver oil (d) Concentrated solutions of vitamin A, D and A and D.	(a) In well-filled, well-closed container. (b) Protected from light <i>Halibut liver oil</i> :—Stored under nitrogen or vacuum.	Unstable—1 year. Vitamin contents. Diminish with rancidity.
7	Vitamin preparations (B complex, C. E. K).	<i>All vitamins except nicotinic acid</i> :— (a) Kept in well-closed containers (b) Protected from light <i>Aneurin hydrochloride solution in acid solution.</i> <i>Nicotinic acid</i> :—Does not need such protection.	All vitamins are fairly stable. Nicotinic acid is the most stable of the lot. Vitamin E is destroyed by rancid fats but otherwise it is remarkably stable.
8	Preparations in a form to be administered parenterally— (a) Bismuth injections (b) Histamine phosphate. (c) Hydrag. salicylate (d) Iron injection (e) Neostigmine methylsulphate injection. (f) Pierotoxin injection. (g) Amylocaine hydrochlor. (h) Quinine dihydrochlor. (i) Morphine injection (j) Sulphadiazine, soluble. (k) Sulphapyridine, soluble. (l) Sulphathiazole, soluble. (m) Hormone injections.	(a) In hermetic container (b) Protected from light	Stable.
9	Preparations containing hormones not in a form to be administered parenterally.	(a) In well-closed container (b) Protected from light	Fairly stable (18 months).
10	Sterilized surgical ligature and suture	In hermetically sealed glass tubes or other suitable container.	Will keep indefinitely.
11	Other injectable preparations.	Kept in well-closed containers	Stable.

Appendix B

Note on the conditions of storage in regard to biological and other special products specified in Schedules C and C(1) to the Drugs Rules, 1945

1. The Sub-Committee appointed by the Drugs Technical Advisory Board to investigate into and report on the conditions of storage in regard to biological and other special products specified in Schedules C and C(1) to the Drugs Rules, 1945, have taken into account the views of the members on this question. The conditions of storage laid down in the standards recognized by the Drugs Act and the Drugs Rules have also been gone into in detail. A statement indicating the ranges of temperature under which biological and other special

products must be stored and other precautions to be taken in their storage has been prepared and is attached.

2. While the Sub-Committee admit that the statement outlines the ideal conditions under which biological products should be stored, they consider that the practical difficulties in this country in achieving the ideal conditions should be taken cognizance of. As is well known, electricity facilities necessary for operating refrigerators are not available in the majority of the mofussil and rural areas in India. The question of employing ice-chests as an alternative arrangement in the absence of refrigerators cannot also be considered as ice may not be available in those areas. Above all, refrigerators are *not at present* available in numbers that will be required.

3. In view of the practical difficulties enumerated above, the Sub-Committee desire that in order *not to hamper* the wholesale and retail drug trade in the country, the conditions of storage for biological products should be such as can be within the practical reach of the dealers. The Sub-Committee therefore consider that the conditions of storage should vary from place to place according to the facilities available. The following arrangements are suggested :—

(a) *Capital cities such as Madras, Bombay, Calcutta, etc., where facilities are available for cold storage.*—All wholesale dealers of drugs in such places should be required to equip their premises with the ideal conditions of storage. Thus, they should have refrigerators wherever cold storage arrangements are indicated in the statement prepared by the Sub-Committee and a specially cooled dry room well-protected from light for the storage of Schedule C(1) drugs.

In the case of retail dealers also, the same conditions of storage should be insisted upon.

However, in the case of *retail dealers*, if it is proved to the satisfaction of the licensing authority that refrigerators could not be secured despite earnest attempts to do so, such dealers could be permitted to use ice-chests or other mechanically operated refrigerators by which sufficient refrigeration conditions could be achieved. Wherever ice-operated or mechanically operated refrigerators are employed, the licensing authority *must* not allow more than three months' stocks of items requiring refrigeration in order to ensure that large stocks do not get deteriorated owing to lack of proper storage conditions.

(b) *District towns and other fairly developed mofussil areas : Wholesalers and retailers.*—Wherever electricity facilities are available, refrigerators must be insisted upon. *In the absence of electricity* or if electrically driven refrigerators are not available, ice-boxes or mechanically operated refrigerators may be allowed for ensuring proper temperature conditions in which case, however, the stocks maintained at any time should not exceed three months' requirements.

(Note.—The Sub-Committee is, however, of the opinion that wherever the licensing authority considers that mechanically operated refrigerators are as efficient as electrically operated ones, it should be left to his discretion not to insist on only three months' stocks being maintained by the dealer.)

(c) *Rural areas and other places which are not electrified or where no ice is available or can be made available.*—In such cases, it has been the experience that the normal room temperature in cool dry places well protected from light, particularly in underground vaults, is generally between 20°C. and 25°C. even in the hottest part of the year. It is therefore suggested that in these areas, items requiring both cold storage and cool storage arrangements, may be kept in cool dry underground vaults and should be well protected from sun light. Since the consumption in these areas is not likely to be much, it may be advisable to restrict the stocks of items requiring cold storage and cool storage and to lay down that stocks of such items should not exceed three months' consumption. Items like tincture digitalis and extract ergot liquid should preferably be kept in 2 to 4 oz. well-closed bottles.

The Sub-Committee, however, felt that this relaxation should be permitted only as a temporary measure and for three years in the first instance, after which period this question should be re-examined.

4. Closely linked with the question of storage of biological and other special products is the question of arrangements to be made for the transport of perishable drugs in such a way as to preserve their potency and properties during transit. For this, the ideal conditions would be to arrange for the movement of biological and other special products by fast transports in cold storage vans so that the risk

of exposure to high temperatures may be minimized. While air transport is quick, it is not likely to become popular until the air freight charges are reduced to a reasonable level. As regards railway transport, there is, however, hardly speaking, any regular arrangement for cold storage vans in fast-moving trains. The Committee are of the opinion that it will benefit considerably the Indian manufacturers of drugs as well as importers of foreign drugs if cold storage arrangements are introduced in fast-moving trans-country trains. The Railway Board should be apprised of the facts and asked to consider the feasibility of such cold storage arrangements being introduced in their transport. Incidentally, it is pointed out that apart from helping the movement of perishable drugs, such arrangements are sure to be welcomed by other industries also such as the Fish Industry, Fruit Industry, etc. Pending the introduction of cold storage accommodation in train services, the Committee recommend that the following practical arrangements may be suggested to the manufacturers and importers of the drug trade :—

- (i) Biological and other special products can be sent by fast passenger train packed in airtight packages. This would reduce the period of exposure of consignments to the ravages of climatic conditions.
- (ii) Clearance arrangements at the consignor and consignee ends should be prompt.
- (iii) A liberal exhibition of labels in various Indian languages, such as, 'keep in a cool place', 'stow away from heat and sun' on the packages should go a long way in reducing the risk of deterioration during transit.

5. The Committee also consider it worth while making enquiries from leading importers in this country representing foreign manufacturers in the U.K., U.S.A., Australia, Switzerland, Canada, etc., as to what storage arrangements are available for the transport of biological and special products by air and on board the ships.

LONDON CONFERENCE OF E.N.T. SPECIALISTS

(From Release Nos. B.F. 1639 and 1668 issued by the British Information Services, New Delhi)

MORE than 1,300 delegates, including about 900 specialists in ear, nose and throat diseases from 39 countries, are now in London attending the Fourth International Conference of Otolaryngology. India is represented by four delegates—Dr. C. A. Amesur of Bombay, Dr. Miss C. M. Leelavathi of Madras, Lieut.-Colonel P. Papatla of Cuttack and Dr. D. Ram of Patna.

The Congress programme is packed with readings of scientific papers, with technical discussions and with visits to hospitals and clinics.

The patron of the Congress is the King, and it was opened on his behalf by the Duchess of Kent. The President is the celebrated surgeon, Mr. V. E. Negus.

By the time the Congress ends, the delegates will have heard the results of clinical and research work in otolaryngology throughout the world.

Dr. C. A. Amesur will be returning home with a number of new ideas, especially in regard to the fenestration operation for deafness for which a completely new technique has been developed in Britain.

Dr. Amesur, who is the President of the Association of Otolaryngologists of India, said that the interchange of experiences at the Congress was most fruitful.

Dr. Miss C. M. Leelavathi (of Madras) spoke of her visit to Britain as a revelation of British medical and hospital efficiency. She was especially interested in British medical films.

Public Health Section

INCIDENCE AND CONTROL OF KALA-AZAR IN THE EASTERN DISTRICTS OF UNITED PROVINCES

By B. G. PRASAD, M.D. (Luck.), D.P.H. (Cal.),
D.T.M. (Cal.)

Assistant Epidemiologist, United Provinces, Lucknow

KALA-AZAR as a distinct clinical entity has been recognized in this country for about a century. A number of epidemics occurred in Bengal, and though it was in early stages confused with malaria, failure to respond to specific treatment led to the establishment of its separate entity. This was confirmed in 1903 by the discovery of Leishman-Donovan bodies—the causative organism, by W. B. Leishman in the spleen of a soldier who died in England from kala-azar which he had contracted at Dum Dūm and by C. Donovan in Madras in material from spleen puncture carried out on patients believed to be suffering from malarial cachexia (Scott, 1942). It invaded Assam in 1875, and swept up the Brahmaputra valley in three different epidemics between this date and 1917 (Napier, 1946). In Bihar, there was an epidemic of kala-azar in 1939-41 and the province suffered heavily from its ravages (Sen Gupta, 1947). It now seems to have slowly infiltrated the eastern districts of United Provinces during the last 25 years. According to Napier (*loc. cit.*) the disease is endemic in this province as far west as Lucknow, where the infiltration gradually tails off, its westerly extension being checked by the dry areas. Sporadic cases have even been reported from the Punjab, Delhi, Jaipur and Mussoorie (Heilig and Sachdev, 1947; Amir Chand *et al.*, 1948).

The heavily infected districts in the United Provinces, so far known at present, are Gorakhpur, Deoria, Basti and Banaras. In Banaras City, the Municipal Board opened a kala-azar dispensary in the year 1932-33. In Gorakhpur district, first survey of kala-azar was done in 1938. Two rural development travelling dispensaries in this district and one in the district of Banaras at Sakaldiha were opened in 1942 for the heavily infected areas. In 1944, some survey work was done in Basti district as well. With the increasing movement of labour and army personnel in the last Great War to Assam, Bengal, North Bihar and back, the disease, as shown (table I), started showing signs of rapid increase in the eastern districts and measures for its control had to be rapidly intensified and widely organized, covering nearly the whole of eastern part of the province.

It is seen that since 1941-42 the disease has shown a rapid rise in the districts of Banaras (specially municipality), Gorakhpur and Deoria.

TABLE I

Number of kala-azar cases treated in certain eastern districts of the United Provinces

Year	Gorakhpur and Deoria districts	Banaras district	Banaras municipality	Basti district
1935	270	201
1936	221	242
1937	240	287
1938	208	115
1939	191	260	152	..
1940	247	306	287	..
1941	202	597	429	30
1942	559	536	398	42
1943	1,263	827	690	35
1944	3,030	960	945	100
1945	3,901	905	878	243
1946	5,200	1,332	1,222	281
1947	8,455	1,355	1,232	880

The rise in Basti was recorded a little later. (Increased facilities provided for diagnosis and treatment in the districts may be, at least in part, responsible for the considerable rise in the figures in 1946 and 1947.) The reasons for this rise may be :—

1. Movements of labour and army personnel from the eastern districts of United Provinces to Assam, Bengal and Bihar during the last Great War and their returning with the infection. In January 1946 it was reported by the Assistant Director of Medical and Health Services, IV Range, Gorakhpur, that as many as 1,000 labourers were daily coming from Assam to Gorakhpur and he proposed that they might be examined for kala-azar in the labour camps and arrangements be made for treatment of those found positive.

2. The endemic and in some areas epidemic prevalence of kala-azar in the adjacent province of Bihar and its slow infiltration to the eastern districts of this province.

3. High density of population in the eastern districts as a whole and abnormal congestion of Banaras City in particular.

4. The prevailing climatic and socio-economic conditions in the eastern districts favourable for the propagation of the transmitting vector, the sand-fly *P. argentipes*, such as comparatively high humidity and low mean diurnal range of temperature, alluvial soil with large tracts under wet cultivation, ill-ventilated houses built out of mud, and poor economic condition.

Present position and control

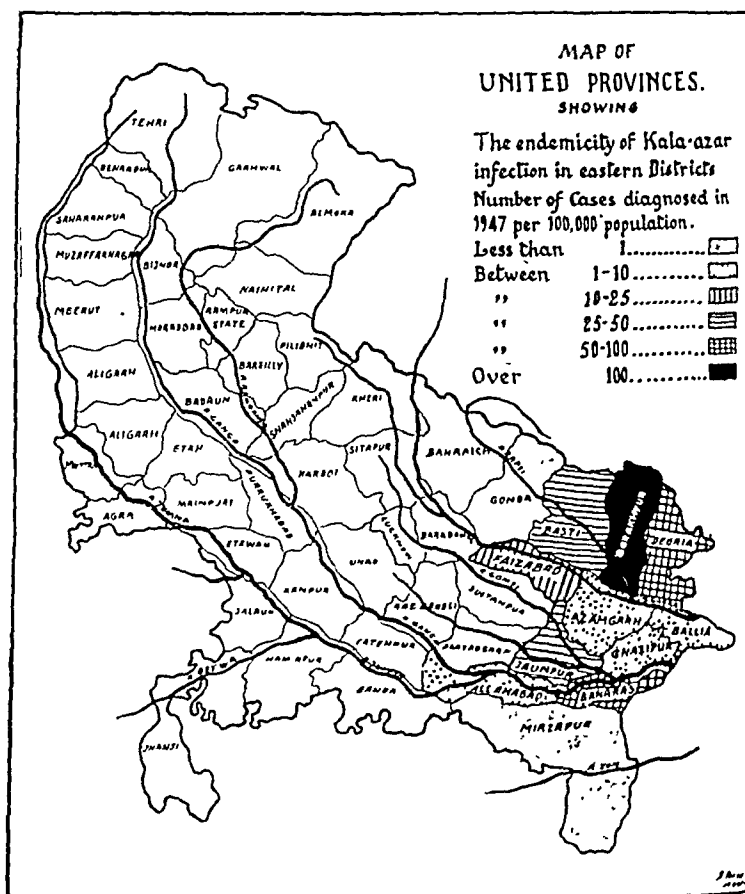
Thus kala-azar became a major public health problem in the United Provinces, and demanded much more vigorous measures by the State to

eradicate the disease than the detailing of a couple of travelling dispensaries here and there. Early detection and treatment of cases being the primary control measure, the first step was to gauge its intensity in different districts in order to get an idea of the magnitude of the problem. Control of sand-fly in rural areas is rather a difficult problem and cannot be much of a success without improving the housing condition and surroundings. Early treatment campaign is effective and is the cheapest method of eradicating the disease.

In November 1945, some stock of urea stibamine was supplied to branch and mill dispensaries in Gorakhpur, Deoria, Banaras and Basti districts, the medical officers having been trained earlier in the technique of diagnosis and treatment of kala-azar at district hospitals. One wholtime medical officer was also posted in 1945 for survey work in the district of Basti. More outdoor dispensaries were opened in Banaras municipality. District-wise data were collected in 1945-46 and a comprehensive scheme was drawn up early in 1947 for an organized anti-kala-azar campaign in the eastern districts. Government realizing the urgency of the problem had sanctioned in 1946 the starting of twenty non-mechanized travelling dispensaries to cover remote rural areas and also the equipping and providing of free facilities for diagnosis and treatment in the existing branch and mill dispensaries of the eastern districts. Liberal supply of urea stibamine was placed at their disposal. Ninety-nine fixed dispensaries were equipped by 1947. Eleven of the non-mechanized travelling dispensaries also started functioning by September 1947 in these districts. These dispensaries have been put in the charge of medical graduates and their scale of pay is Rs. 300-25-400-30-700-50-850 p.m. A peon and a coolie are allowed to each travelling dispensary. Tents have been provided for camping in rural areas. A non-recurring expenditure of Rs. 2,000 was incurred to provide tents and furniture and a recurring expenditure of Rs. 5,500 per annum is provided on pay, allowances and contingencies for each travelling dispensary. Besides this, a sum of Rs. 50,000 is annually provided in the provincial budget for the purchase of urea stibamine, distilled water, kala-azar outfits and medicines of common ailments for supply to the various treatment centres from the Epidemic Stores Depot, U.P., Lucknow. The medical officer in charge of travelling dispensary visits villages for survey in the morning and treats cases in the afternoon at his camp headquarter. The unit is usually stationed for three months in one area. Portable kala-azar diagnostic and treatment outfits which can easily be carried by a coolie (size 16 inches by 11 inches by 10 inches) have been provided to all the treating centres. The outfit contains some 33 items of equipment and is self-sufficient for diagnosis by serum tests (formol-gel and urea stibamine tests) and treatment. Prescribed

forms for collecting and reporting of the monthly data and printed instructions on treatment and diagnosis were distributed to all the treating centres. An elaborate case card has also been introduced. To get a rough idea, village-wise information of cases is also collected in each district through vaccinators and *patwaris*. A kala-azar sketch map (1 inch = 4 miles) has been prepared for most of the districts and the area has been divided into convenient circles for being assigned to the fixed and travelling dispensaries. The anti-kala-azar campaign, thus, was put on a firm footing and an organized start made in 1947 in the affected districts. Work done during 1947 is shown in table II and district-wise intensity of infection based on the number of cases diagnosed in 1947 is shown in the map. This map will need to be revised when figures for next ten years or so become available.

MAP



Monthly reports from all the treating centres are received by the District Medical Officer of Health on the prescribed forms giving information about each case. The district figures are reported monthly to the Assistant Director of Medical and Health Services of the Range and the Assistant Director of Epidemiology. Regular monthly spraying with D.D.T. in the infected localities as an anti-sand-fly measure is also being carried out. Besides, a permanent sanitary gang of a jamadar, two coolies and two sweepers provided in each tahsil, temporary coolies are

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trained and engaged, whenever necessary for syringing work. Propaganda is done by the district health staff and by the Health Publicity Bureau, which has prepared a talkie film and a pamphlet on the disease. Regulations under the Epidemic Diseases Act, 1897 (III of 1897), making it compulsory for a person suffering from kala-azar to take the treatment, have not been enforced, as the experience of this measure in Bihar has rather been disappointing.

District-wise progress

The anti-kala-azar scheme is functioning at present in the districts of Gorakhpur, Deoria, Banaras, Basti, Jaunpur, Azamgarh, Ballia, Ghazipur, Allahabad, Faizabad and Mirzapur (table II).

six dispensaries are providing free treatment in the city. There is not much of kala-azar in the Banaras rural areas at present. In 1942, in 106 villages surveyed only 11 cases were detected and in 1943 in 180 villages surveyed 48 cases were detected. One hundred and ten and 123 cases were treated in 1946 and 1947 respectively in the rural areas of the district.

In 1944 and 1945 one wholetime medical officer was deputed to survey the heavily infected areas in Basti district. Heavy infection was reported in the northern parts of the district. A survey covering about two months showed that 37 villages were infected and as many as 242 cases were detected in 9 villages. The writer had an occasion recently to survey in some detail an infected village, Pokhara, situated in the

TABLE II

Showing kala-azar work in eastern districts of United Provinces in 1947

Name of the district	Number of circles in which the districts has been divided	Number of fixed dispensaries acting as diagnostic and treatment centres	Number of kala-azar travelling dispensaries proposed for the district	Number of kala-azar travelling dispensaries functioning during 1947	Number of bloods examined by aldehyde and antimony tests by all agencies during 1947	Number of bloods found positive for kala-azar by serum tests during 1947	Number of cases diagnosed in 1947 per 100,000 population	Number of cases treated during 1947	Number of villages surveyed during 1947	Population surveyed during 1947	Worst affected areas in the district
1. Gorakhpur ..	24	16	4	3	7,195	7,075	318.0	7,075	103	55,500	Maharajanj and Pharendra tahsils.
2. Deoria ..	22	17	4	1	1,965	1,482	85.2	1,380	44	57,159	Padrauna and Hata tahsils.
3. Banaras ..	11	10	3	3	2,040	1,335	99.1	1,355	157	99,950	Banaras municipality.
4. Basti ..	24	10	5	1	1,036	911	40.4	880	267	42,800	Bansi tahsil.
5. Jaunpur ..	16	8	1	1	853	423	28.5	326	126	41,800	Shahganj tahsil.
6. Azamgarh ..	19	11	2	1	157	62	3.1	52	40	14,500	Ghosi tahsil.
7. Ballia	6	23	23	2.0	23
8. Ghazipur	5	68	62	5.7	55
9. Allahabad	4	1	1	119	73	3.6	89	12	5,046	Meja tahsil.
10. Faizabad	10*	2†	..	145	143	10.3	143	Akbarpur tahsil.
11. Mirzapur	12	25	8	0.8	12
TOTAL	109	22	11	13,635	11,597	..	11,390	749	316,755	..

N.B.—No cases were reported from the districts of Gonda, Bahraich and Bara Banki during the year 1947.

*Ten fixed dispensaries started doing kala-azar work in 1948.

†Two kala-azar units have also been proposed for this district.

Preliminary survey carried out on cases attending dispensaries in 1945 in the districts of Gorakhpur and Deoria showed that the disease was fairly widespread particularly in Maharajanj and Pharendra tahsils in the former district and in Padrauna and Hata tahsils in the latter district. In 1946, 5,200 cases were treated by the various dispensaries in the two districts. Kala-azar has been endemic in Banaras City for a long time, showing a sharp rise since 1941. At present

interior, some 6 miles from Basti City. A report was received from the President, District Board, that a large number of people had died from tuberculosis in this village. A preliminary visit by the District Medical Officer of Health showed that the disease affecting the village was kala-azar.* The writer visited this village in December 1948 for a detailed report. It is

* Will those f... of epi' please note. M.G.

of tub-

situated on the edge of a big marshy *Tal* (2½ miles by 1 mile). At the time of the visit the area surrounding the village was dry but during rains it gets flooded. The subsoil water level was at 15 feet and during rains it rises to 10 feet. Crops grown in the surrounding area are mustard, sugarcane, wheat and barley. The village has a population of 987 (884 Hindus and 103 Mohammedans). Twenty-two kala-azar cases were diagnosed by serum tests at the time of the visit. One bed-ridden female, aged 30 years, very strongly positive by serum tests, with history of eight months' fever, liver four fingers and spleen two fingers, very much emaciated and having diarrhoea, also showed Leishman-Donovan bodies in the peripheral blood. One case of fever, negative by serum tests, was positive for malaria parasites.

Enquiry into socio-economic status showed that with the exception of some two dozen houses of *Thakurs*, the village is inhabited by *Chamars*, *Kumhars* and *Julahas*. Nearly all are cultivators. Out of the 182 families living, 177 (97.2 per cent) are poor (monthly income less than Rs. 100) and five (all *Thakurs*) are middle class (monthly income between Rs. 100 and Rs. 500). The houses of the latter group were inspected in detail by the writer and were found to be *kutchas*, insanitary, ill-ventilated, dark, in bad state of repairs and had cattlesheds adjoining them. There had occurred twenty-five deaths from suspected kala-azar in these five families of *Thakurs*. Three cases were present at the time of the visit. One of these families of 33 members (present strength), the richest in the village, had as many as 14 deaths and had one case under treatment in the district hospital. This shows that all are equally liable to infection when living under insanitary conditions. 75 per cent of the houses in the village have thatched and 25 per cent tiled roofs. All houses except three are single storeyed. Even in them, the upper storey is not used for living. Except two houses all were ill-ventilated and badly lighted. Torch had to be used for entering most of the living rooms visited during the day time. Except half a dozen houses all were in damaged condition and needed renewal of mud plaster badly. Twenty-two houses (12.1 per cent) had kala-azar cases at the time of visit and more than 50 per cent of the houses gave history of deaths from suspected kala-azar in the past. There was 512 head of cattle accommodated in 196 cattlesheds attached to 135 houses (74.2 per cent) in the village. All the cattlesheds were insanitary and in bad state of repairs. The cowdung is allowed to accumulate for some days before it is removed from the cattlesheds. The village presented insanitary appearance and as many as 95 rubbish heaps were counted in the village. The sanitation was good only in 21 houses (11.5 per cent).

Out of 163 children examined, 14 (8.6 per cent) had enlarged spleen. Seventy-seven

children of the primary school in the village were also examined for clinical signs of deficiency diseases; two had angular stomatitis and six Bitot's spots.

No definite history could be elicited as to how the epidemic started in this village. Information was, however, obtained that at least four persons of this village had served in Calcutta and Howrah for a number of years and suffered from prolonged illness and fever. One of these aged 25 years, who died about 14 years ago, was employed in some Bengali family on cow feeding for ten years in Calcutta. He used to come to the village regularly every 1½ to 2 years. When he last came about 15 years ago, he died after an illness for about 1½ years with fever and enlarged spleen. Another villager employed in Howrah returned ill, after some years' stay about ten years ago, with fever and enlarged spleen. Two other villagers working in Calcutta for a number of years returned ill last year with history of prolonged fever and died after some days' stay in the village. The disease, it appears, first started in eastern part of the village inhabited mainly by *Chamars* and *Kumhars*. Some sixteen houses adjoining each other in this locality gave history of kala-azar cases and 32 deaths occurring in a population of 121 persons between 1944 and 1948. The disease then spread to the rest of the village and lately, *Thakurs*, who are economically better placed but have the largest number of cowsheds and are living in insanitary, though big, houses like others, suffered heavily. In three adjoining houses of *Thakurs*, as many as 33 persons out of 53 persons living, died from prolonged illness and fever between 1946 and 1948. In another house, 14 persons died between 1946 and 1948 (see above). These houses were free before 1946. In nine years (1940 to 1948), some 129 persons had died from the disease in the village. Year-wise deaths from suspected kala-azar cases (based on house-to-house enquiry) were (deaths are shown in the bracket): 1940 (1), 1941 (3), 1942 (4), 1943 (4), 1944 (14), 1945 (20), 1946 (25), 1947 (38) and 1948 (20). It appears that the peak of the epidemic was reached in 1947 and now it is on the decline.

A hurried survey in the adjoining villages within a distance of one mile from village Pokhara gave 9 positive cases in 7 villages. One treatment centre has now been opened in this area and a systematic survey is being carried out.

Till July 1946, the district of Jaunpur was considered to be a relatively free district. With the co-operation of the medical officers of the fixed dispensaries and private practitioners, 102 cases were diagnosed and 67 treated from September to December 1946. Seventy-six cases were also detected in 152 villages surveyed in 1946-47. In the remaining districts so far only few cases of kala-azar have been reported.

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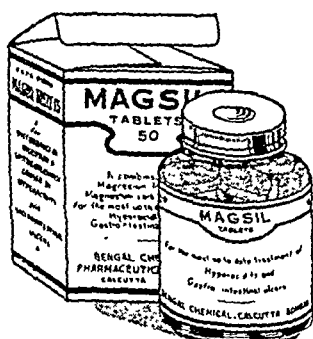
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Summary

1. Kala-azar at present is confined to eastern parts of the United Provinces. An attempt has been made with the available data to show the distribution of kala-azar in these parts where lately it has been showing a rise in its incidence. The figures available for each district have been discussed to show the degree of its endemicity. Some of the districts have definite belts of heavy infection. Data of a village in district Basti, where an epidemic outbreak has occurred, are discussed in some detail.

2. Measures undertaken for control are discussed. Necessary machinery has been provided in eleven eastern districts through the agencies of 109 fixed and 22 kala-azar travelling dispensaries (of which 11 have started functioning). During 1947, out of 13,665 bloods examined by serum tests, 11,597 were found positive and 11,390 cases were treated. Seven hundred and forty-nine villages were surveyed by the medical officers in charge of kala-azar travelling dispensaries. Thus, a regular anti-kala-azar scheme has been strated in the affected districts and a good amount of work is now being done.

The writer thanks Dr. A. C. Banerjee, Director, and Dr. A. N. Das, Deputy Director of Medical and Health Services, United Provinces, for encouragement to write this article. His gratitude is also due to the latter for some very useful suggestions.

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The Indian Medical Gazette Fifty Years Ago

LONDON LETTER

BOOM IN TROPICAL MEDICINE

(Reprinted from the *Indian Medical Gazette*, Vol. **34**, June 1899, p. 215)

THE boom in tropical medicine waxes louder. The Edinburgh and Aberdeen Universities are establishing lectureships on the diseases of tropical climates. The Liverpool School has been started on promising lines, and the London School is being diligently organized. The staff of the Dreadnought Hospital at Greenwich have resigned their appointments, and considering the

securvy manner in which they have been treated by the Committee of the Seamen's Hospital Society, this is not surprising. Meantime, the branch at the Albert Docks is being enlarged for the purpose of accommodating an increased number of patients to serve as clinical material for the new school. Funds are forthcoming in sufficiency to defray the cost of these enlargements, and it is anticipated that the amount originally estimated as necessary to launch the institution in an efficient state will be realized. A banquet is to be held on the 10th of May for the purpose of inaugurating the school; the Colonial Secretary is to preside, and many distinguished men—among them the Marquess of Lorne, Lord Lister, Lord Rothschild, Lord Strathcona, the Lord Mayor of London and Sir Donald Currie—have consented to attend. The function will, therefore, be an impressive one, and will, as is usual on such occasions, be distinguished by an outpouring of eloquence, and it is to be hoped a loosening of purse strings. Dr. Patrick Manson has worked the scheme with energy and success. A great number of tropical practitioners have testified in the medical journals regarding the benefit they have gained from attending the practice of the Albert Dock Hospital in its embryo state, and when the school has been put into full working order, the quantity and quality of the instruction derivable from it will be greatly enhanced. The *Journal of Tropical Medicine* has reached its eighth number, and gives evidence of strong vitality. It is further proposed to start a society for the discussion of tropical diseases in London. With all these facilities for gaining information regarding maladies peculiar to the tropics, and the peculiarities of ordinary diseases in tropical climates, it is a cause of wonder how men who practised in tropical countries in times past gained the knowledge necessary to enable them to do so.

Riding the tropical hobby too hard

A correspondent of the *Lancet*, writing anonymously from South Africa, has the hardihood to affirm that all this special education is not requisite, and that an intelligent and attentive student can obtain, during his curriculum of study in any medical school, sufficient training in the principles and details of medical science to enable him, with the aid of textbooks, to recognize tropical diseases readily when he encounters them and to treat them successfully. He asserts that he himself found no difficulty in so doing. There is some truth in this view, and it may be that the tropical hobby is being ridden rather hard. But whatever may be said as to the possibility of obtaining a theoretical acquaintance with tropical diseases without seeing them, there can be no denying that a practical familiarity derived from observation of cases and study of objects is infinitely superior to more or less hazy notions derived from books and lectures; and

the application of general doctrines to particular and hitherto unseen phenomena is apt to result in misapprehension. Moreover, the comparison with times past is unsound, because investigation on the spot has revealed circumstances and conditions governing the causation, pathology, course and treatment of tropical diseases which could not possibly have been discovered otherwise, and this accession of knowledge has come to constitute a large body of special science which must be mastered, if any advance is to be made on the same line, that is, by observation and research *in loco*.

Tropical disease outside the tropics

And this special study throws light not only upon tropical disease in the tropics, but also on tropical disease occurring outside of the tropics. For example, the knowledge which had been gained in the tropics regarding beri-beri must have been very helpful to the medical superintendents of the lunatic asylums in Europe and America, in which this disease has made its appearance.

Dysentery in English asylums and jails

Similarly, the occurrence of outbreaks of dysentery in the same class of institutions may well be studied in comparison with the prevalence and fatality of this disease in Indian prisons. The most severe epidemic of dysentery which I ever witnessed was in the Durham County Asylum while serving there as Assistant Medical Superintendent during the years 1861-64. The cases were mostly of the diphtheritic or croupofibrinous type, very severe and fatal. The outbreak occurred about the same time as that which happened in the Cumberland and Westmoreland County Asylum, the incidents of which were so fully and ably described by Dr. Clouston in the *Lancet* at the time. In both instances the disease was undoubtedly due to faulty sewage disposal, especially to the irrigation of fields with the putrid contents of sewage tanks. No doubt the enfeebled systems of the patient rendered them more apt to succumb to infection and perhaps crowding and other sanitary defects arising from the accumulation of insane persons contributed to the result. With a vivid recollection of these events I perused with very great interest the excellent leader in your February issue on 'Dysentery in English Asylums and Indian Jails'. There was a time when dysentery was a scourge of English prisons. Dr. Baly's account of his experiences in the Millbank Prison is historical. Improved sanitation has banished the disease as well as typhoid fever from English prisons, and there can be no question or doubt that dysentery is capable of being banished from English asylums and Indian prisons by similar means. Dr. Gemmel has done well in bringing this subject into prominent notice; and although the conditions

which originated and spread dysentery in Indian prisons are more difficult to deal with them in similar institutions in temperate climates. Efforts to abate the scourge must be unrelenting.

The cause of cancer

The April number of the *Practitioner* is devoted exclusively to the subject of cancer, and contains information of the most interesting and important character regarding the prevalence, distribution, localization, grouping, possible infectiousness and microbic origin and treatment operative and otherwise of that justly dreaded malady. The articles are contributed by men who have made these special phases of the subject a special study, and within a moderate compass one may obtain the most recent and exact information on each of the topics which I have specified. Mr. Malcolm Morris did a very good work in devoting a special issue of his journal to tuberculosis, and thus contributing materially to initiate and promote the great movement which has arisen, having for its object the prevention and, if possible, suppression of tuberculous infection. The circumstances, as regards our knowledge of cancer causation, are not such as to justify a similar crusade; but good will undoubtedly come of directing special attention to points connected therewith, which are eminently and urgently deserving of attention and further investigation.

Current Topics, Etc.

Tetanus from Kaolin

(From the *Pharmaceutical Journal*, Vol. 160, 12th June, 1948, p. 406)

Two cases of tetanus in newly-born children have recently been reported in the *British Medical Journal* (22nd May, p. 980) and in both cases the use of a 'Baby powder' is suggested as the source of the infection, although in only one instance was it possible to culture *Cl. tetani* from the powder and the post-mortem material. The powder has been used to sprinkle on the umbilical stump. On enquiry, it was found that the suspect powder contained kaolin, magnesium silicate, boric acid, and perfume, and of these ingredients only the kaolin yielded an anaerobic spore-bearing bacillus. Such cases are uncommon in Britain, although a series of similar infections which were traced to a dusting powder have recently been reported from New Zealand. If the cause were, in fact, the use of infected kaolin, the occurrence should receive the widest publicity, for makers of dusting powders ought to be aware that such preparations are frequently applied to lesions of the skin and the presence of pathogenic organisms in any of the ingredients may give rise to septicæmic conditions. The sterilization of most powders is a simple matter provided no decomposition occurs in heating, and with an inert substance such as kaolin, it should be a routine practice to sterilize by heating at 150-160°C. whenever the substance is likely to be used as an application to the tissues.

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Original Articles

GRANULOSA-CELL TUMOUR OF THE OVARY

A BRIEF REVIEW OF ITS IMPORTANT CHARACTERISTICS AND A REPORT OF 12 CASES

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OVARIAN neoplasms continue to be an ill-understood chapter in oncology. From the large class of them can be separated out a distinct group comprised of granulosa cells and theca cells and distinguished by characteristic clinical manifestations, histological structure, and functional activity.

Historical.—Though the earliest reports of the granulosa-cell tumour can be traced as far back as 1855, some of them may not conform to the type as understood now, because a variety of tumours containing what were believed to be ova-like inclusions were grouped in a single class (Geist, 1942). von Kahliden (quoted by Geist, 1942) described his 'adenoma carcinomatosus folliculare' in 1895 and he traced its origin to the primordial follicles of the ovary. von Werdt (quoted by Geist, 1942) was the first to suggest that these tumours arose from Walthard's granulosa-cell strands and he coined the name granulosa-cell tumour. To Meyer (1931), however, must go all the credit for separating out the granulosa-cell tumour as a specific entity and for describing its distinct, though varied, histological features. Since then, a large number of cases have been reported in the literature and the granulosa-cell tumour can no more be considered a rare neoplasm of the ovary. In this country, case reports have been published by Khanolkar (1943) and Menon and Veliath (1943).

Nomenclature.—Among the various names given to this neoplasm may be mentioned: follicular adenoma, fibroma ovarii adenocysticum, folliculoma ovarii malignum, carcinoma folliculoides, adenocarcinoma folliculoides, cylindroma, granulosa-cell tumour, and granulosa-cell carcinoma. The name granulosa-cell tumour appears to be the most accepted one. Novak (1947), however, has suggested that because of their common origin from ovarian mesenchyma already differentiated as female, both the granulosa-cell tumour and the theca-cell tumour should be included under the common designation 'feminizing mesenchymoma of the ovary'.

Clinical characteristics.—The highest incidence of the granulosa-cell tumour is between 30 and

60 years (Ewing, 1941). The youngest patient reported in the literature is an infant 9 months old (Lull, 1941) and it also occurs at a very late age. According to Novak and Gray (1936), though this tumour is common after the menopause, the highest incidence is during the reproductive period. On the other hand, Bland and Goldstein (1935) found that its incidence during the reproductive period and after the menopause was the same, while Dockerty and MacCarthy (1939), in their series, encountered 60 per cent of the cases after the menopause.

Small silent nodules have been discovered at the autopsy (Ewing, 1941). More commonly, because of the functioning tissue of the neoplasm, the symptoms are striking, and, at times, even dramatic when it occurs in the pre-pubertal or the post-menopausal periods. A varying period of amenorrhœa followed by metrorrhagia or meno-metrorrhagia is a common symptom during the reproductive period and at this age period the real significance of such symptoms is easily missed. In the pre-pubertal period, the clinical manifestations consist of precocious puberty—precocious menstruation, precocious development of the secondary sexual characters, and accelerated skeletal growth (Novak, 1933, 1947; Novak and Gray, 1936). In women, in the post-menopausal period, the symptomatology is equally striking: uterine bleeding from a mere spotting to the establishment of a more or less regular anovulatory menstrual cycle together with enlargement of the breast, and maybe rejuvenation of the sexual desire. Novak (1947), however, has denied that any effects could be produced on the secondary sexual characters, because, at this phase of life, the organs concerned have ceased to be receptive to the usual hormonal stimuli. The uterine bleeding stops after removal of the tumour and a second menopause with its accompanying vasomotor symptoms has been observed (Schulze, 1933). The uterine bleeding, both in the reproductive period and the post-menopausal period, may re-appear due to the recurrence of the tumour to disappear again after removal of the recurred growth. All these peculiarities are explained by secretion of the follicular hormone by the functioning neoplastic cells. Among the non-specific symptoms are swelling of the abdomen and pain, and complaints due to pressure of the tumour mass on the adjoining structures.

Physical signs include presence of an adnexal mass, enlargement of the uterus, and ascites in case of large and highly malignant tumours. Meigs's syndrome has been observed (Rodgson, Dockerty and Mussey, 1945). The general signs due to hormonal disturbance have been mentioned above. Pre-operative estimation of the œstrogen content of the blood and the urine shows an increase and is helpful in diagnosis. Endometrial biopsy may show hyperplasia and in the case of a tumour with atypical histology the

finding is an aid in correct diagnosis (Ewing, 1941).

Pathology.—The granulosa-cell tumour makes from 1 to 10 per cent of all ovarian tumours seen in various clinics (Ewing, 1941). More than 90 per cent of the granulosa-cell tumours are found to be unilateral (Dockerty and MacCarthy, 1939). There is wide variation in their size. The smallest reported is 4 millimetres in diameter (Hodgson, Dockerty and Mussey, 1945); the largest weighs 34 pounds (Dockerty and MacCarthy, 1939). Those of moderate size are usually well circumscribed and solid. The larger growths may show, on the cut surface, shallow cystic cavities filled with yellowish or brownish fluid. Areas of hæmorrhage and necrosis are common in these. Usually the cut surface has a greyish white colour with shades of distinct yellow, in patches, due to luteinization. At the operation, extension to the fallopian tubes, broad ligaments, coils of intestine and the peritoneum has been described (Hodgson, Dockerty and Mussey, 1945).

Microscopic characteristics.—The histological characteristics are the most important criteria for the diagnosis. The pattern varies not only in different tumours but even in different portions of the same tumour. The amount and the mode of distribution of the connective tissue in the neoplasm partly governs the production of the different histological variants. These are (1) folliculoid type, divisible into micro- and macro-folliculoid forms, (2) cylindromatous, (3) pseudo-adenomatous, and (4) parenchymatous, which, at times, may assume a sarcomatous appearance. The pattern of the individual tumour is identified by the predominant architecture noted after examining several blocks made from different areas of the mass. Whatever the prevailing pattern, the general morphology of the neoplasm remains the same. The constituent cells resemble the granulosa cells of the ovary and have growth characteristics identical with those of the granulosa tissue. The cells may be small and embryonal, or large and polyhedral; rarely they are cylindrical and in the sarcomatous type they are spindle-shaped. The cell membrane is indistinct and the cytoplasm clear, faintly granular, or foamy. The nucleus is round or oval, vesicular, and contains moderate amount of chromatin. Nucleoli are conspicuous. Whatever the pattern, the cells show a tendency to arrange themselves in rosettes or clusters with central lumina, some of which show a pink-stained mass. The appearance is the result of granular and hydropic degeneration of the central cells but the resemblance to primordial follicles and the Call-Exner bodies of rabbits is great and these features are very characteristic of granulosa-cell tumours. In between the groups of epithelial cells is the stroma usually fibrous and moderately vascular. Quite a large proportion of granulosa-cell tumours show theca-cell areas at the edges of

the epithelial cell-masses (see figure 4, plate XXI). The epithelial cell-masses, themselves, may show various grades of luteinization in patches. Rarely, the luteinization is complete, giving rise to the commonest type of luteoma. Reticulum staining is helpful in differentiating granulosa-cell tumours from the theca-cell tumours. Traut *et al.* (1939) and Henderson (1942) have shown that in the granulosa-cell tumour the reticulum is sparse and surrounds small and large groups of epithelial cells, while, in the theca-cell tumour, the individual cells are enclosed by the reticulum.

The neoplastic cells do not contain any glycogen or mucin. Special staining for fat, according to the technique of Hoerr-Römeis, reveals different kinds of fat. However, it is doubtful whether this is of much help in differentiating the granulosa-cell tumour from the theca-cell tumour, as was once thought (Hodgson, Dockerty and Mussey, 1945). The biologic activity of the granulosa-cell tumour may have some relationship to its cholesterol and phospho-lipoid content. Both are increased when there is luteinization (Hodgson, Dockerty and Mussey, 1945). Though no quantitative assays have been reported so far, presence of oestrogen has been demonstrated in the tumour tissue.

The dominant pattern in the neoplasm gives no indication of its probable behaviour. Nor are the cytologic criteria for defining the degree of malignancy very reliable, and many authorities have emphasized their failures in correlating the histological appearance of the neoplasm with its behaviour clinically. On the other hand, Ewing (1941) has remarked, 'the statement that there is no relation between the structure and the clinical course may well be referred to lack of experience of the observer and the failure to consider the age of the patient and the extent of the disease'. The clinical malignancy has been appraised by various workers to vary from as low as 6.4 per cent (Hodgson, Dockerty and Mussey, 1945) to as high as 28.1 per cent (Novak and Gray, 1936). Though the growth of the neoplasm is usually slow, recurrence after removal may be quick; on the other hand, Jones and TeLinde (1945) have reported recurrences as late as after 15 to 20 years. Usually the recurrence is local and local extirpation of the recurred growth may result in a permanent cure. Metastases have been recorded in various organs: the other ovary, abdominal viscera, retroperitoneal lymph nodes, pleura, meninges and bones (Ewing, 1941; Soltman, quoted by Geist, 1942). On the whole, however, the granulosa-cell tumour must be reckoned among the relatively benign neoplasms.

Relationship of the granulosa-cell tumour to endometrial hyperplasia and uterine carcinoma.—The hyperœstrinism produced by the functioning cells of the tumour leads to endometrial

hyperplasia. The endometrium is in the proliferative phase and the glands show cystic changes, resulting in the characteristic Swiss-cheese pattern. The association of the granulosa-cell tumour with endometrial carcinoma has been recorded by many observers (Ingraham *et al.*, 1944; Stohr, 1942). It has been attributed to the continuous oestrogen stimulation of the endometrium. Similarly fibromyomas of the uterus and fibroadenomas of the breast (Ackerman and del Regato, 1947) and even carcinoma of the breast have been concurrently reported (Hodgson, Dockerty and Mussey, 1945).

Histogenesis.—The prevalent concept of the histogenesis of the granulosa-cell tumour is based upon Fischel's thesis of derivation of the real germinal epithelium of the ovary from the mesenchyme of the sex-gland anlage. The granulosa tissue of the ovary is derived from this mesenchyme. Meyer (1931) held that the adult granulosa was incapable of undergoing a neoplastic transformation because of the lack of stimulus of the germ cell upon which life of the granulosa was solely dependent. He upheld the original contention of von Werdt (quoted by Geist, 1942) that the neoplasm was derived from embryonal cell-rests, the 'granulosa ballen'. Novak (1947) contended that this thesis was not tenable in its original form and that the origin of these neoplasms could be traced to a still earlier stage of granulosa-cell development—the pro-granulosa and the pre-thecal phase from the primitive mesenchyme. At this stage, the cells had assumed feminizing characteristics but had not yet differentiated into granulosa and thecal tissues. This explained, according to him, the common occurrence of both granulosa and thecal cell elements in the same tumour. This view of the mesenchymal origin of the granulosa-cell tumour was supported by Geist (1935). Geist, Gaines and Pollack (1939) further proved the mesenchymal derivation by experimental production of these neoplasms in mice by irradiation.

Material and methods

The ovarian neoplasms received in the department during the years 1931 to 1947 were re-studied to discover the incidence of granulosa-cell tumours. In the older cases, paraffin blocks alone were available for examination. In the recent cases the tissue had been preserved and a more detailed examination was possible. The diagnosis of this tumour in our material has been made mostly on the histological appearance. Hæmatoxylin and eosin staining and reticulum staining were done in every case. Staining for fats to confirm the presence of areas of luteinization was possible only in the more recent cases. The case records were scrutinized for relevant information.

Results

Clinical history.—Of the 12 cases encountered in 1 no history was available. The ages of our

patients varied from 18 to 53 years. No case was met with in the pre-pubertal period; 8 were in the reproductive period, and 3 in the post-menopausal period. One patient was an unmarried woman, 1 was a young widow, and the rest had from 3 to 7 previous conceptions. Two patients did not have any menstrual irregularity, 3 complained of scanty menses during a period from 6 months to 1 year prior to admission, and 6 had either increased or abnormal bleeding for periods varying from 4 months to 3 years. Of these latter, 3 in the reproductive period gave a history of meno- or metrorrhagia; the other 3 had had their menopause some time back and reappearance of uterine bleeding was their chief complaint. Four patients complained of 'pains in the stomach'; in 1 patient this was of severe type and in attacks recurring every few days. In this case the neoplasm was found to have perforated the small intestine. Abdominal swelling for a few weeks to 4 years had been noted by 9 patients. Constipation was mentioned by 2 patients without special questioning. Two patients had difficulty in micturition, 1 had difficulty in breathing and 1 had œdema of the feet.

On abdominal examination, a mass was palpable in 9 instances. It varied in size in individual cases from a 'small nodule' in the hypogastrium to a 'lump' reaching the umbilicus. In 3 cases the consistency of the mass was recorded as 'tense cystic'; in 6 as 'solid'. Clinically, free fluid in the peritoneal cavity was not detected in any patient. Examination per vaginam showed a large bulky uterus in 3 cases. The additional information gathered at the time of operation was as follows: small quantities of serous fluid in the peritoneal cavity in 2 cases and of sero-sanguineous fluid in 3 cases; the tumour was adherent to the uterus in 4 cases; in 1 case the peritoneum was riddled with tubercles (verified histologically later); and in 1 case the tumour had perforated into the small intestine (see figure 5, plate XXI). In this last case the only indication of this happening was the history of severe attacks of abdominal pain recurring every few days.

Pathological findings.—The largest tumour in this series weighed 2,280 grammes. In 2 instances the neoplasm was bilateral. Seven of the neoplasms (including the 2 bilateral cases) were solid; in 1 case solid and cystic components formed almost equal portions of the tumour mass; and in 2 the neoplasm was so riddled with small cysts that it could only be described as cystic, though a few solid greyish areas could be made out here and there. In 2 cases the naked-eye appearance of the tumour was not recorded.

The histological findings are detailed in a tabular form (see table). It will be seen that in 4 cases the predominant pattern was the parenchymatous (see figure 1, plate XXI);

TABLE
Histological findings

Serial number	Histologic type	Rosettes and Call-Exner bodies	Theca-cell areas	Luteinization	HISTOLOGIC EVIDENCE OF MALIGNANCY		
					Variation in cell size and shape	Mitotic figures	Infiltration of capsule
1	Parenchymatous	Present	Few	Present in patches.	Present	Few	Present (also of the fallopian tube). Absent
2	Parenchymatous	"	Absent	"	Absent	Occasional	"
3	Cylindromatous	"	Few	Absent	"	"	"
4	Parenchymatous and cylindromatous.	"	Present in large numbers.	"	"	"	"
5	Parenchymatous	"	"	Present in patches.	"	"	Present
6	Micro-folliculoid	"	Few	"	"	"	Absent
7	Parenchymatous	"	"	"	"	"	"
8	Parenchymatous and cylindromatous.	"	Present in large numbers.	An occasional area.	"	"	"
9	Macro-folliculoid and cylindromatous.	"	"	Absent	"	"	"
10	Cylindromatous	"	"	"	"	"	"
11	Cylindromatous and micro-folliculoid.	"	Few	"	"	"	"
12	Micro-folliculoid	"	Absent	"	Present	Present in moderate numbers.	Present; had infiltrated the small intestine.

in 2 the cylindromatous (see figure 2, plate XXI); in 2 the micro-folliculoid (see figure 3, XXI); in the remaining 4 cases there was a mixture of the different patterns that no single one could be called predominant.

The endometrium was available for study in a single case and it showed the characteristic hyperplasia. In 1 case there was associated tuberculous salpingitis and peritonitis.

Summary and conclusions

1. The important features of the granulosa-cell tumour are briefly reviewed.

2. A series of 12 cases encountered during a period of 17 years is reported.

3. Only one-half of the patients in the series gave a history of abnormal or excessive bleeding per vaginam.

4. The ultimate diagnosis of this neoplasm is by histological examination.

5. In 1 case the neoplasm was found associated with tuberculous salpingitis and tuberculous (dry) peritonitis. In another case the neoplasm had perforated the small intestine. In 2 cases it was bilateral.

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EXPLANATION OF PLATE XXI

Fig. 1.—Photomicrograph showing the parenchymatous pattern. H.E. X about 400.

Fig. 2.—Photomicrograph showing the cylindromatous pattern. H.E. X about 300.

Fig. 3.—Photomicrograph showing the micro-folliculoid pattern. H.E. X about 400.

Fig. 4.—Photomicrograph showing the theca-cell areas (stained pale). H.E. X about 300.

Fig. 5.—Photograph of the specimen. The neoplasm has perforated into the small intestine.

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BIOSYNTHESIS OF ASCORBIC ACID IN HUMAN BEINGS

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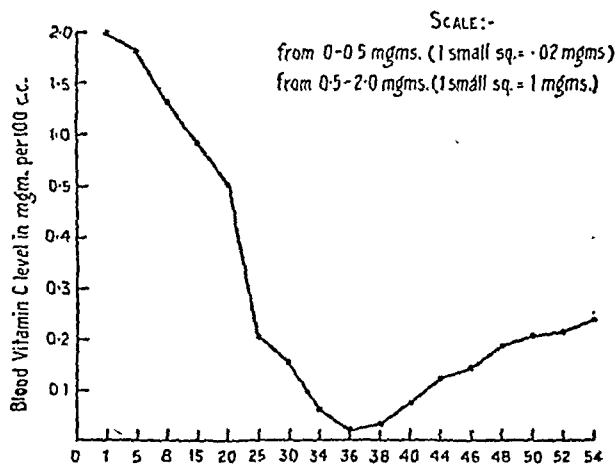
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Introduction.—It is generally recognized that human beings, monkeys and guinea-pigs do not synthesize vitamin C in their body. The difference in the time of onset of the symptoms of vitamin C deficiency were attributed to differences in age, sex and locality. The great extent to which pregnant women could tolerate vitamin C deficiency could not be explained. It has, however, been suggested that possibly the foetus synthesizes vitamin C and that this is the cause of higher tolerance levels in the case of pregnant women. The fact that nursing mothers secrete more vitamin C in their milk than they consume has been assumed to be due to biosynthesis of vitamin C by them. What is the actual state of affairs in normal non-pregnant women and in men does not appear to have been studied. The possibility of biosynthesis of vitamin C in them has been examined in the present series of investigations.

Experimental technique and material for study.—Six normal healthy girl students and 4 healthy males between the ages of 16 and 25 were selected. The level of vitamin C in blood was estimated in every case before the experiment was started. The cases included men and non-pregnant women, 6 of whom were vegetarians and 4 taking a mixed diet. The method used was the volumetric method of Farmer and Abt in which the plasma proteins are precipitated with metaphosphoric acid and the ascorbic acid in solution titrated with standardized 2:6 dichlorophenol indophenol-sodium solution. The above volunteers were then kept on a regulated

vitamin C free diet. Vitamin C content of the blood was studied at regular intervals. The volunteers were also clinically examined regularly and any symptoms of vitamin C deficiency noted carefully.

A graph showing mean average figures of the changes in blood vitamin C level of ten volunteers kept on vitamin C deficient diet for two months.



Number of Days on Vitamin C deficient Diet and on which the blood of the Volunteers for Vitamin C Analysis was drawn.

Discussion of results

As will be observed from the graph, there is a gradual decline in the vitamin C content of the blood on the vitamin C free diet given to the volunteers. This decline reaches the lowest level on an average in 36 days. Although this period differs from individual to individual, a time does come when every individual reaches a minimal level. It is after this minimal level has been reached that the quantity of vitamin C in the blood begins to rise and this continues for about 18 days. Here also there is an individual variation and every individual has his or her own time limit up to which a gradual rise continues. It is generally during this period that symptoms of vitamin C deficiency manifest themselves and further experimentation had to be discontinued on account of the reluctance of the volunteers to undergo further investigations.

It therefore appears that when a minimal level of vitamin C in blood has been reached human body tries to overcome this deficiency by synthesizing vitamin C itself or there might be a rush of vitamin C from the tissues in the blood to maintain a minimal level. In any case the rise in the level of blood vitamin C is not sufficient to withstand deficiency symptoms and the small response which may be due either to synthesis or exchange is insignificant.

Summary

1. Vitamin C content of the blood of 10 human volunteers kept on vitamin C deficient diet was examined.

2. It has been found that there is a gradual decline for a definite period up to 36 days the minimum vitamin C level in the blood in mg. per 100 cc. blood reaching 0.02 mg., after which there is an average rise to a maximum of 0.23 mg. per cent in blood.

The writer is indebted to Professor S. N. Mathur, ph.D. (Lond.), Professor and Head of the Department of Physiology, Lucknow University, for suggesting this, still unexplored, problem and for his continued help throughout the course of this work.

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A CASE OF MENINGITIS DUE TO HAEMOPHILUS INFLUENZAE

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MENINGITIS due to *H. influenzae* is not an
unusual finding especially in a child. It has

sera and streptomycin in such cases have been published. In India except in large city hospitals, bacteriological investigation even of hospital cases is not often possible and much less so in private practice. In view of the rarity of such an investigation, with positive findings of *H. influenzae*, it was thought proper to report the following case :—

Case report

A female child, aged six months, admitted in a private nursing home with a history of low fever for 15 days, irritability and occasional convulsions, was seen by a physician at this stage. Kernig's sign positive. There was some rigidity of the neck. Lumbar puncture on 9th December, 1948; C.S.F. purulent under pressure. (The other laboratory investigations are given below.)

Treatment.—Treatment was started with intramuscular and intrathecal injections of penicillin. Fever came down but rigidity and convulsions increased. Second lumbar puncture was done on 17th December, 1948; C.S.F. findings as before. Sulphadiazine two tablets four-hourly given. Fever kept at 99°F., there was marked opisthotonos. Third lumbar puncture was done on 29th December, 1948; C.S.F. much less turbid. Case continued with remissions and relapses with meningeal symptoms. Patient was further given intramuscular and intrathecal injections of streptomycin. Patient had three changes of physicians since admission to the nursing home and was removed against advice before recovery. Attempts to trace him have failed.

Laboratory investigation

C.S.F. was examined by one of us (V. H. S.) on three occasions and the results are tabulated below :

	9th December, 1948	17th December, 1948	28th December, 1948
Quantity ..	7 cc.	5 cc.	5 cc.
Appearance ..	Turbid, deposit and coagulum present.	Same as before	Faintly turbid. No deposit.
Proteins ..	Increased	Increased	Increased.
Chlorides ..	600 mg. per cent	610 mg. per cent	610 mg. per cent.
Sugar ..	Diminished	Diminished	Diminished.
Microscopic— Cells ..	610 per c.mm. polymorphs predominate.	410 per c.mm. polymorphs predominate.	110 per c.mm. polymorphs few.
Organisms (Gram's and acid-fast methods). ..	Not seen	Gram — ve bacilli seen in smears.	Stray Gram — ve bacilli seen.
Culture ..	Gram — ve bacilli grown ? <i>H. influenzae</i> .	Colonies of Gram — ve bacilli in fair numbers. No acid-fast bacilli.	No growth.

been reported by many workers in Europe and America and the strains isolated have been studied. The reports about the effects beneficial or otherwise of various sulpha group of drugs with and without anti-haemophilus specific

The direct smears and the culture of the second lumbar puncture C.S.F. were brought to the senior author for opinion. The smears showed fair numbers of intra- and extra-cellular Gram-negative, pleomorphic bacilli with halo

round them suggestive of a capsule and they resembled atypical *H. influenza* which appear predominantly in bacillary or filamentous forms with swollen and bulbed portions. Culture on blood agar being rather old showed similar but faintly stained organisms. These were subcultured in glucose broth and on to a blood agar slope. There was no growth in glucose broth. Out of the three colonies subcultured on different part of the same agar slope, only one grew. The colonies in further subculture were tiny, transparent, smooth and shiny like 'S' forms of *H. influenza*, and were non-hæmolytic. The organisms were further tested in different media with the following results :

and studied was atypical *H. influenza* requiring both 'X' and 'V' factors, showing slow and scanty growth on blood agar, not producing hæmolysis, and differing from typical strains in showing predominantly bacillary or filamentous morphology with swollen and bulbed portions and a halo suggestive of a capsule. It stained feebly with counter stain in Gram's method, a property in common with this group. Indole production was doubtful. No fermentation tests were put up. Virulence test was not decisive, possibly because it was not done with the primary culture or an adequate dose was not administered or a sufficient number of animals was not used. Colonial characters were those

Medium	Result	Remarks with regards to 'X' and 'V' factors in the media
1. Glucose broth	No growth	'X' and 'V' factors absent.
2. Blood agar with <i>Staph. aureus</i>	Discrete but crowded colonies as described before, round the <i>Staph.</i> colonies.	Both 'X' and 'V' factors present.
3. Same as 2, but with penicillin	No growth of either	'X' alone (from blood).
4. Glucose broth with <i>Staph. aureus</i>	Scanty growth of bacilli with cocci	'V' alone (from cocci).
5. Same as 4, but with penicillin	No growth of either	'X' and 'V' absent (no blood; no cocci).
6. Chocolate agar slope (prepared by dipping for a minute a blood agar slope in boiling water and resloping).	Profuse but discrete colonies as described above showing morphologically <i>H. influenza</i> in 24 hours.	Both 'X' and 'V' available (from heated RBC).
7. Same as 6, but with penicillin on its surface.	Very scanty growth after 48 hours	The strain appears to be sensitive.

From the growth on chocolate agar slope, subcultures were made as follows to further ascertain its cultural requirements :

of *H. influenza*. The organism was found to be sensitive to penicillin to a certain extent. Bacteriostatic effect of penicillin on a large

Medium	Result	Remarks with regards to 'X' and 'V' factors in the media
8. Peptone water	No growth	No 'X' and 'V'.
9. Peptone water with <i>Staph. aureus</i>	No bacilli but cocci grown	'V' alone.
10. Peptone water with heated blood	Bacilli as described before grown	'X' and 'V' present.

Indole test was carried out with last culture by adding the Roseindole reagent after extracting the culture with ether. A faint pink colour was seen. Thus it was feebly positive. Test was negative on peptone water with heated blood used as control.

Pathogenicity test was carried out with two white mice.

A thick suspension was made in normal saline from chocolate agar, $\frac{1}{4}$ cc. was injected intraperitoneally in one and $\frac{1}{2}$ cc. in the other. Animals looked ill after 18 hours. The one with smaller dose was killed after 24 hours as it appeared more ill. Smears and cultures were made from peritoneal surface and heart blood. No organisms were seen or grown, the other animal recovered.

Discussion

In accordance with the classification given by Wilson and Miles (1946), the bacillus isolated

number of strains of *H. influenza* has now been well established. The bacilli were present in three samples of C.S.F. from the patient on different dates. It was missed in the direct smear first time, probably due to its faintly staining character and atypical morphology.

Pittman's (1931) antigenic study of *H. influenza* in U.S.A. showed that most of the strains from the pathological lesions chiefly meningitis produced characteristic 'smooth' colonies. They were found to be capsulated and formed fairly homogeneous group. Serological types a, b, c, d, e, f have been described by her and type 'b' occurred with the greatest frequency in the cases of meningitis. She also noted that those from the respiratory tract were non-hæmolytic, non-capsulated 'R' forms and serologically heterogeneous and non-pathogenic. Mulder (1939) and Gordon, Woodcock and Zinnemann (1944) have described cases of

purulent meningitis due to 'R' forms. In the absence of facilities for serological typing but judged by the findings in our case it appears that this organism would fall in line with one of the Pittman's serological types. With regard to other findings in C.S.F., it may be pointed out that the cell count should be interpreted in the light of the coagulum formed. Rhoads (1947) in his review of 550 cases of bacterial meningitis noted in connection with meningococcal meningitis that the higher the cell count in C.S.F. the worse was the prognosis, the count usually being in thousands. In the fatal group of *H. influenzae* meningitis, he found the spinal fluid glucose too low to read. Glucose was diminished in our case.

Assessment of the effect of drug in this case was not possible, as the treatment was delayed and the patient was under different physicians and was removed from the nursing home against advice. In spite of the delayed therapy, the patient had remissions and had regained consciousness; relapses were probably due to want of continuity of intensive treatment.

Reference to the literature regarding therapy in *H. influenzae* meningitis would not be out of place here.

The importance of using large doses of sulphonamides and their continued use after meningeal symptoms have disappeared in order to avoid relapses had been stressed by Davies (1943) and Moir (1943). Mutch (1941) and Davies (1943), however, are not impressed by the curative value of these drugs, particularly in infants.

Bolsevert, Fousek and Grossman (1944) have reported successful outcome in three babies with meningitis due to *H. influenzae* type 'b' treated with intramuscular injection of specific anti-*H. influenzae* type 'b' rabbit serum, combined with sulphadiazine. In such cases mortality was 100 per cent prior to the introduction of serum.

Gordon, Woodcock and Zinnemann (1944) described a clinically severe case of meningitis due to *H. influenzae* type 'b' which responded well to sulphapyridine. Patient had three relapses of meningitic symptoms whenever therapy was cut short. They advised the continuation of treatment for some days after clinical cure.

Zinnemann (1946) has analysed 20 cases of *H. influenzae* meningitis, 19 of these were due to type 'b' strain. He found that combined treatment with sulphonamide and penicillin gave definitely better results than sulphonamide alone.

Alexander and Leidy (1947) have reported treatment of 14 cases of type 'b' *H. influenzae* meningitis with streptomycin alone. Ten cases recovered, and in 3 of the 4 remaining cases, failure was proved to be due to bacilli developing resistance to streptomycin during treatment. Specific antiserum and combined sulphadiazine were substituted with success.

Rhoads (1947), in his review and clinical analysis of 550 cases of bacterial meningitis, encountered 15 cases of *H. influenzae* meningitis. All 15 were in infants and children between the ages of 2 months and 5 years and he concluded that combination of sulphadiazine in full doses plus specific serum in as large doses as possible offered the best outlook for the patient. However, streptomycin 2 to 4 gm. daily 100,000 units given alone intrathecally or combined with the above treatment was recommended as the best choice.

No reference to such investigation of *H. influenzae* meningitis in India has been found so far except one case described by Dutta and Baruah (1948). No details as to the morphology or cultural characters of the strain encountered by them are given. They reported having cured it by sulphadiazine orally and injections of penicillin for 5 days till the temperature was completely normal. In view of the relapses noted by various workers and by us in our own case, further observation in their case would have been desirable. They also stated that the strain appeared to be quite unlike the strains investigated and reported by others. That some strains are sensitive to penicillin has been reported in the past. The present strain recovered by us at least was sensitive *in vitro* experiments. In any case, the combination of treatment as advocated appears to be the best.

Summary

In view of the rarity of laboratory investigation a case of *H. influenzae* meningitis is described.

1. Atypical *H. influenzae* was found repeatedly in C.S.F. from this case. It was seen intra- and extra-cellularly with polymorphonuclear leucocytes predominating.

2. The strain was studied morphologically, culturally and for its pathogenicity.

3. The organism stained feebly and was likely to be missed hence special search has to be made.

4. Literature on therapeutics in *H. influenzae* meningitis is summarized with a hope that it may be useful to those interested.

Our thanks are due to Dr. F. G. Shafi for allowing us to report this case from his private nursing home.

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SPORADIC CASES OF ENCEPHALITIS IN RURAL BENGAL

By M. L. KUNDU, M.B., F.R.F.P.S., L.M.

Nabadwip

THE following case notes suggest that cases of *Encephalitis lethargica* occur occasionally in the area including the town of Nabadwip and its adjoining villages in both the districts of Nadia and Burdwan.

9th January, 1949.—The patient, M. M., age 21 years, of village Singhaguri near Sumudragarh, district Burdwan, a healthy young cultivator, came to sell straw in Nabadwip. About noon he went to purchase something in the bazar after selling the straw, when he was, according to bystanders, seized with convulsions and fell down on the road-side. The convulsions persisted for two hours, after which he became unconscious. He lay there throughout the night. His people arrived the next morning on search, found him on the road-side drain* and brought him to my consultation room at about 9 a.m.

Pulse was 68 per minute, regular and of normal volume but slightly increased tension, respiration 16 per minute, and temperature in axilla 101°F. Face was flushed and there was contraction of the pupils on both sides. He resisted attempts to open his mouth but there was no froth nor any sign of injury anywhere. The body was relaxed and there was no Kernig's sign of exaggeration of reflexes or stiffness of the neck. There was no enlargement of the liver or spleen. There were some râles and rhonchi in the chest but no dullness anywhere and the heart sounds were normal. There was no smell of any drug in the mouth and the bladder was empty. Blood: no malaria parasites; W.B.C. 15,000 per c.mm., poly 82 per cent, L.M. 1 per cent, S.M. 16 per cent, eosinophils 1 per cent. Spinal fluid came under pressure but it was perfectly clear.

He was given 4-hourly injections of soluseptasine intramuscularly and glucose 12½ per cent 50 cc. twice a day. Orally no medicine could be administered in the beginning, but later on

* Will the social workers kindly attend to the next case lying unattended by a drain?—EDITOR, I.M.G.

glucose feeds could be given slowly and sulphadiazine powders were given. He made some improvement after 24 hours but died on the fourth day.

12th December, 1948.—Called to see a Mohammedan male child, 4 years of age, in village Gholapara, on the other side of the river on the 4th day of his illness. History of fever starting with convulsions and vomiting and the child becoming unconscious soon afterwards. As usual in medical practice out here, he had been given a quinine injection and some mixture was tried to be forced down the throat, but with no success.

The child was in a state of constant spasm. Pulse 100 per minute, temperature by rectum 101.8°F. No enlargement of the liver or spleen, abdomen and eyes sunken, pupils moderately dilated. No stiffness of the neck or Kernig's sign present. No adventitious sound in the heart or lungs. On lumbar puncture, clear fluid came under pressure and after removal of about 10 cc. the convulsions stopped. An injection of camphor-in-oil was given and rectal feeding with glucose advised, and also glucose intramuscularly. Patient showed some improvement on the next day and could swallow some fluids but started having convulsions the following day. As no one was procurable to do another lumbar puncture, this therapeutic help could not be given and the child died after 3 days.

10th October, 1948.—A Mohammedan male child in Nabadwip Mussalmanpara, aged about a year, reported to have developed fever a week ago and treated as a case of typhoid. Began to get convulsions from the 4th day of the fever and became completely unconscious on the 5th. day. Seen on the 7th day of the illness. Child in a semi-comatose condition, slight stiffness of the neck, temperature 100°F., pulse 140, respiration 20 per minute, abdomen sunken, Kernig's sign present. Blood examined showed no M.P., leucocyte count 13,000 per c.mm., poly 72 per cent, lympho 5 per cent, S.M. 21 per cent, eosino 1 per cent. Pupils moderately dilated on both sides. Rectal feeds were given and bromides by mouth and injections of camphor-in-oil, and on the 8th day the child showed some improvement, with convulsions diminished. As sulphadiazine by mouth and soluseptasine made little improvement, lumbar puncture was proposed but the child's father refused it. On consultation with another practitioner, streptomycin was started and even after 3 days there was no improvement and the child became opisthotonos. A lumbar puncture under chloroform now brought out clear fluid without much pressure and it did not improve the condition. The child eventually died on the 15th day.

14th August, 1948.—Hindu male, 20 years, at Nabadwip Poramatola, was seen in consultation with another practitioner on the 3rd day of the disease, with history of high fever ranging between 103 to 104°F. and the patient having

convulsions and gradually getting comatose. Quinine intramuscularly had been given already and repeated without any benefit. On examination the extremities were cold, and patient lethargic. Pulse 140, temperature by rectum 107°F., respiration 30, no adventitious sounds in the heart and lungs, no stiffness of the neck, Kernig's sign absent. Blood examined, no M.P., leucocytes 14,500 per c.mm., poly 73 per cent, S.M. 24 per cent, L.M. 3 per cent, eosino 2 per cent. Was put on wet pack and later ice enema. Glucose given intravenously and cartazol injections repeated every 4 hours. At night another medical man was called without notice, who gave another quinine injection and the patient died very soon afterwards. Pupils were contracted equally.

21st May, 1948.—A Hindu female child, 2 years, at Nabadwip Ramsitapara, seen in consultation with another medical man on the 3rd day of the illness. History of high fever and convulsions, unabated with usual treatment, with purgative, sponging and bromides. Pulse 158, respiration 34, abdomen sunken, pupils moderately dilated, temperature 102°F. by rectum, Kernig's doubtful, slight retraction of neck, no adventitious sounds in heart or lungs. Quinine already given by injection. Lumbar puncture showed clear fluid under pressure and convulsion stopped after this. No treatment was of any avail and the child died after two days. Blood examination revealed moderate leucocytosis and no malaria parasite.

Comments

The picture of this series of cases confronts us with a disease which is characterized by fever and convulsions or coma followed by the signs of meningitis, like retraction of neck, Kernig's sign being either absent or present in a doubtful manner. The disease proved fatal in 3 to 15 days. Injection of quinine, soluthiazole or streptomycin did not make any impression and in fact injection of quinine made them worse than before and proved fatal in one case. It had the common character of the spinal fluid being under pressure and removal of it stopped the convulsions. The fluid was absolutely clear and showed no increase in the cellular elements. Blood showed in every case moderate leucocytosis with increase of polymorphs but not to the extent we get in cases of cerebrospinal, pneumococcal or influenzal meningitis. There was no rash or any evidence of exanthematous condition to group it with virus diseases like typhus, measles or any septicæmic conditions. Further elucidation could have been made of its nature, if there was a possibility of doing a spinal fluid or blood culture, both of which are not possible in this town at present.

From facts gathered from the rural practitioners during the last 4 years of my stay in this province, I have been told often by them that these are cases of malignant malaria and that

they do not hesitate at all to give in such cases quinine intramuscularly without making any attempt to take a blood slide and have it examined beforehand. Of course, out in the villages it will be a counsel of perfection to have a blood examination done, as not even 5 per cent of our rural population can afford either the cost of it or the means of taking blood slides to towns where a microscopical examination could be done. On the top of it very few medical men can take proper blood films for the purpose and the quacks that abound have no qualms on their conscience about the need of a diagnosis. In our town, however, where there are several medical men trained in laboratory work or at least possessing a microscope, it should not be impossible to have a couple of slides taken before quinine is pushed by injections, and it seems that the fear of missing a case of malignant malaria is always predominant in our minds so that we do not think of other possibilities.

I am presenting a dismal array of a subtle disease, probably of virus nature, unamenable to our present armamentarium of antibiotics and certainly of fairly wide distribution in our town and villages, which requires a diagnosis. The nearest approach to my mind is that these are cases of *Encephalitis lethargica*, though they do not conform to the classical description. But it is well known that the signs and symptoms vary very much in different localities.

FILARIAL EOSINOPHILIOSIS

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THE prevalence of transitory pulmonary infiltrations has been noted by many workers all over the world. Loeffler in 1932 described such transitory pulmonary changes demonstrable roentgenologically associated with a high eosinophilia. This association of pulmonary infiltrations and eosinophilia was also described by Weingarten in 1943. He called this syndrome, 'Tropical eosinophilia'. The most characteristic features of his series of cases observed in Bombay were marked eosinophilia (33 to 81 per cent), paroxysms of asthma and fleeting pneumonic infiltrations demonstrable radiologically.

Loeffler believed that the cause of the condition was a specific pulmonary reaction to a variety of antigens and hence he thought it was an allergic manifestation. Jayawardena in 1945 demonstrated mites in the sputum of 11 out of his series of 21 cases of this syndrome. Van der Sar had two cases in 1946 in which Loeffler's syndrome existed and which he demonstrated as cases of pulmonary ascariasis.

The present writer has recently observed cases of filariasis both in children and adults in whom Loeffler's syndrome was present. In most of these cases micro-filariae were demonstrated in the peripheral blood (2, 3 and 5). Some of the cases furnished other clinical evidence of filariasis such as elephantiasis, hydrocele and orchitis. Lung involvement was demonstrated roentgenologically in all the cases. Most of these cases complained of asthmatic attacks or wheezing. Eosinophils were present in the sputa of cases 1, 2, 3, 6 and 7. All had marked eosinophilia in peripheral blood with more or less leucocytosis. Case 8 is interesting because the Loeffler's syndrome appeared to be due to *Tenia solium* infestation. The picture is typical and this case had a stormy convalescence due to developing a spontaneous pneumothorax.

The present series of cases stresses the importance of filariasis in the causation of asthma and the development of transitory pulmonary infiltrations.

Clinical features

Filariasis may give rise to a variety of clinical conditions such as 'filaria' fever (cases 1 and 6), lymphangitis, lymphatic varices, enlarged lymph glands, elephantiasis (cases 2 and 6), chyluria (case 6), lymphuria, orchitis (case 1), chylocele (case 8), funiculitis abscess, arthritis, synovitis, chylous ascites and chylous diarrhoea. The cases in the present series have one constant finding of asthmatic attacks. These attacks are best described as wheezing. The patient himself is conscious of this wheezing and those who are near him also are conscious of the wheezing. The wheezing is almost constant but appears to be much worse during the morning.

Filarial fever is a fairly common manifestation of filariasis. This fever does not respond to sulphonamides or penicillin and this lack of response suggests that filarial fever is not due to secondary bacterial infection.

The early signs and symptoms of the disease are perhaps allergic in nature as stressed by Loeffler. This allergic reaction appears to involve the lymphatic tissue. These early changes are therefore reversible as distinct from the irreversible changes seen in late chronic disease with heavy infestation which are probably due to the direct mechanical or inflammatory obstructive effects.

Diagnosis

Diagnosis is made on the clinical manifestations: Confirmation of the diagnosis is obtained only by demonstrating micro-filariae. But micro-filariae are not usually found in the blood during the earlier months of the disease. It appears that several months are required for the worm to mature and for the completion of the cycle

in the human host. In later months it is, as 'a rule, easy to demonstrate micro-filariae'.

Intradermal test with filarial antigen has been used in more than one series. Fairly found it a satisfactory method of diagnosis. In another series, Michael in 1944 found that the test was positive in 90 per cent of the infected individuals. The present writer has no experience with the intradermal test.

Eosinophilia in the blood is nearly always present. The present series of cases are of interest because these cases show pulmonary eosinophilosis. The chief complaint of all the patients studied was asthmatic attacks. It is, therefore, interesting to note that filariasis should be considered in the aetiology of allergic asthma.

Treatment

Filariasis is a self-limited disease. There is no known anthelmintic against filaria. But recent reports of the use of arsanamide and hetrozan are encouraging.

Culbertson and Rose found that antimony preparations, in large amounts, destroyed the adult worms of *W. bancrofti* in a high proportion of patients. But the dose needed was large and too close to the toxic level.

Hewitt and his co-workers in 1947 discovered 'hetrozan' which is 1-diethylcarbonyl-4-methylpiperazine hydrochloride. In experimental filariasis, hetrozan produces rapid disappearance of micro-filariae from peripheral blood. Santiago-Stevenson and his colleagues in 1947 have carried out clinical trials in West Indies and it appears that hetrozan may prove to be definitely curative.

The drug is given by mouth and the dose employed is from 0.5 mg. to 2 mg. per kg. body-weight thrice daily for 3 to 20 days.

Toxic symptoms are few and mild such as headache, general malaise, weakness, pain in the joints and anorexia.

[* In endemic areas children often show signs of filarial disease and in many of them micro-filariae can be demonstrated. Iyengar showed presence of micro-filariae in children aged 2 years, Sweet and Pillai in a child under one year and in 2 children aged 1 year, in South India. Leiper found filarial infection in a child of 14 months and in 3 others under 2 years, of age in British Guiana. These data show that children are as susceptible to filarial infection as adults and that the incubation period of filariasis is not several years as was previously thought. The reports from the Pacific during the last war also support this view. Moreover, symptoms of filariasis may be often present and yet micro-filariae may not be found in children as well as in adults. Diagnosis of filariasis is therefore yet clinical and examination of blood for micro-filariae may not always be taken as an absolutely essential step.

Incidentally the paragraph dealing with treatment of filariasis has little bearing on the subject-matter of the paper.

Nevertheless, this paper is interesting as the author has suggested that filariasis should be taken into consideration in discussing the aetiology of asthma.—
Editor, I.M.G.J.

Case records

Case 1.—S. B., a man aged 42, was admitted to the Irwin Hospital, New Delhi (service of Lieutenant-Colonel P. C. Dhandra, Associate S. L. Malhotra), on 17th February, 1948, with 10 weeks' history of following illness: Occasional hæmoptysis, fever, attacks of wheezing, inability to raise the right arm and orchitis. He has had 3 previous attacks of epididymo-orchitis, the first at the age of 12, first recurrence at the age of 14 and second recurrence at the age of 34 years. Physical examination revealed rhonchi scattered over both lungs, loss of function of the right circumflex nerve and right-sided orchitis. Skiagrams taken at weekly intervals during his stay showed soft, fleeting pneumonic infiltrations in both lungs. The last skiagram of the series showed deflation collapse of the right middle lobe. Laboratory examination revealed W.B.C. 12,800, eosinophilia 50 to 56 per cent and moderate anæmia.

His sputum was repeatedly negative for tubercle bacilli but was full of eosinophils. Micro-filariae could not be demonstrated in peripheral blood.

The patient continued to have fluctuating fever and attacks of asthma. His orchitis subsided after two weeks of hospitalization. He had another attack of severe orchitis in the same testicle after a week and this testicle burst after two days. The discharge was milky. No micro-filariae found in that discharge. Follow-up after 4 months, chest cleared up, no asthmatic episodes, eosinophilia 20 per cent.

Summary.—A man of 42 had asthmatic symptoms and fluctuating fever. He had marked eosinophilia. Skiagrams of chest showed soft fleeting infiltrations of both lung fields. Micro-filariae not demonstrated. Patient belonged to a filarial district and had attacks of orchitis.

Case 2.—In June 1946, a man of 23 while residing in a filarial district developed an intermittent temperature rising up with a chill. He was in a hospital where his peripheral blood did not show any malaria parasite. He had marked eosinophilia. His temperature did not respond to treatment with quinine and he left hospital after 8 days to try indigenous treatment. Strangely enough, as soon as he left hospital, his temperature came down and remained normal until December 1946. At this stage he started complaining of heaviness in his right leg and in the course of one week developed typical elephantiasis of his right leg.

In September 1947, he had an operation performed for his elephantiasis with an uneventful recovery.

He was first seen by me in December 1947, complaining of asthmatic attacks and fluctuating fever coming on with chills. He had an eosinophilia of 60 per cent. His sputum was full of eosinophils. Actively motile micro-filariae

were recovered from his peripheral blood after repeated attempts. A series of x-rays of his chest over a three-week period showed soft fleeting pneumonic infiltrative shadows, most marked near the lung roots.

Summary.—Man of 26 suffering from filariasis showed Loeffler's syndrome. He also had a history of elephantiasis. The Loeffler's syndrome was associated with filarial fever.

Case 3.—N. K., a girl aged 13, became ill in February 1947, with cough, expectoration and wheezing. She was hospitalized in May, 1948 for the third time in the King George's and associated hospitals, Lucknow, where active micro-filariae were demonstrated in her peripheral blood. She had scattered rhonchi all over her chest. The sputum was full of eosinophils. Blood counts showed W.B.C. 12,000, eosinophils 60 per cent.

Skiagrams of the lungs showed soft infiltrative shadows which cleared up after 3 weeks. Her asthma responded to a course of stovarsol.

Summary.—Girl aged 13, had recurrent attacks of cough, expectoration and wheezing. Micro-filariae demonstrated in peripheral blood. She had a marked eosinophilia. Eosinophils present in sputum in large numbers. There was no other clinical evidence of filariasis.

Case 4.—J. C., a boy of 8, was admitted to the King George's Hospital, Lucknow, in May 1948, with the complaints of cough and expectoration occasionally and wheezing, duration 2 years.

A year ago he had a tonsillectomy performed without any effect on his symptoms. Six months ago he was discovered to have nasal polypi which were removed again without any effect on his wheezing.

On examination the boy was found to have a hydrocele. The chest revealed scattered rhonchi all over both lungs. Sputum examination was negative for tubercle bacilli repeatedly. Skiagram of the chest showed no lesion.

He had a marked eosinophilia 58 per cent. There were no eosinophils in his sputum. Repeated examinations of peripheral blood did not demonstrate micro-filariae.

His asthmatic attacks responded temporarily to a course of stovarsol.

Summary.—Boy of 8 suffered from asthmatic attacks. He belonged to a highly endemic filarial district. He had hydrocele, marked eosinophilia and a history of nasal polypi. Sputum showed no eosinophils. No micro-filariae were demonstrated. Filariasis is a very common cause of hydrocele. Nasal polypi are a common association of Loeffler's syndrome.

Case 5.—B. C., male child, aged 6 years, was brought to the King George's Hospital, Lucknow, in May 1947, complaining of wheezing since October 1946. He had a slight cough with mucoid expectoration which he mostly swallowed.

Examination revealed rhonchi in the chest. Otherwise the child appeared healthy.

He had the following pertinent laboratory findings: W.B.C. 18,300, eosinophils 40 per cent, sputum did not show eosinophils. No tubercle bacilli in sputum and gastric lavage.

Actively motile micro-filariae demonstrated in his peripheral blood.

W.R. ++, Kahn's test negative. X-ray showed no abnormality.

Summary.—Case of eosinophilia aged 6 years. Micro-filariae present in peripheral blood. This case is very interesting as it does not substantiate the observations of Neumann in 1945 who believes the micro-filariae are usually not found before the seventh year after infection has occurred. This child is only 6. Dickson *et al.*, in 1943 however could demonstrate micro-filariae in 1.6 per cent of 244 children under 5 years of age.

Case 6.—H. K., man of 25 years of age, was admitted to the Railway Hospital, Jubbulpore, on 5th September, 1948, with a history of asthmatic attacks of three weeks' duration, irregular febrile episodes of a week's duration, and chyluria of two months' duration.

(He gave a history of passing milky urine in 1946 also. Old case reports revealed that he was treated for malarial fever at that time and also that repeated attempts to demonstrate filariasis had failed.)

Physical examination revealed as follows: Temperature 100°F. Lungs showed scattered rhonchi and a few crepitations. System review showed no other abnormality.

Laboratory findings revealed as follows: W.B.C. 10,000 c.mm., eosinophils 80 per cent, urine was milky in appearance and showed albuminuria, no cells.

Peripheral blood showed actively motile micro-filariae which were so numerous and so constant that slides made at any time of the day or night were found to be full of them.

Sputum showed eosinophils. No acid-fast organisms seen.

Screen examination of lungs showed diffuse mottling of lung parenchyma.

Clinical impression and diagnosis, filarial eosinophiliae.

A week after hospitalization the patient developed swelling of both the feet and ankles.

The patient was treated with neostibosan. His asthma responded to treatment and the lung shadows cleared up.

The patient was called for a follow-up two months later. It was seen that the swelling of the feet had disappeared completely.

Comments.—The case illustrates that the early elephantiasis is probably allergic in nature as it is reversible as distinct from the irreversible changes seen later in disease which are probably

due to the direct mechanical or inflammatory obstructive effects.

Case 7.—Man aged 27 was admitted to the Railway Hospital on 15th September, 1948, complaining of attacks of wheezing and fever of three days' duration.

Physical examination showed scattered rhonchi over both lungs. Skiagrams of the chest revealed diffuse mottling.

Laboratory findings—W.B.C. 11,000, eosinophils 70 per cent.

On the third day of hospitalization the patient suddenly became very ill. He complained of severe abdominal pain, was markedly dyspnoeic and his pulse was rapid and feeble.

System examination revealed spontaneous pneumothorax on the left side. To relieve the patient's dyspnoea air was removed with the help of a pneumothorax apparatus but within two hours the patient again became collapsed and markedly dyspnoeic. Air was again removed with only a temporary relief. It was concluded that he had developed a tension pneumothorax and so a needle with a rubber tube dipping in sterile water was used for decompression.

Thoracoscopy could not be done.

On the third day of the accident the patient felt better and he passed a few segments of a tapeworm in his stool. A sterile, straw-coloured effusion developed on the left base.

He was treated with Ext. Felix and a 30 feet long *Tania solium* with its head was recovered.

The patient had an uninterrupted convalescence. Slight basal effusion was still present at the end of 8 weeks but he had no subjective complaints.

Comments.—Evidently the asthmatic attacks, diffuse pulmonary mottling, a high eosinophilia and *taniasis* appear to be related as after the vermifuge treatment these findings disappeared. It is probable that these manifestations were of the nature of allergic reaction to *Taniasis*.

My thanks are due to Lieut.-Colonel P. C. Dhanda under whose care case 1 was admitted and to Lieut.-Colonel B. L. Taneja for permission to report the case, Dr. B. B. Bhatia, Dean, University of Lucknow, for permission to report cases 3, 4 and 5 and Dr. S. N. Lahiri, Chief Medical Officer, G. I. P. Railway, for permission to report cases 6 and 7, and Dr. L. J. Hiyale, Pathologist to the Railway Hospital, Jubbulpore, for assistance in laboratory work.

ROAD SICKNESS

By H. CHANDRA, P.C.M.S.

Civil Surgeon, Kangra, East Punjab

Road sickness is a well-known entity like sea and air sickness but seldom finds a mention in medical literature. Having extensive experience of travelling both in the plains and hills, I have had opportunities for studying the phenomenon

of road sickness from the medical point of view. Moreover, being subject to this malady myself and having frequently observed the plight of persons suffering from it, I need no apology to dilate upon this condition, basing my remarks on personal experience and observation.

Etiology.—Road sickness is essentially caused by stimulation of the vestibular nerve endings in the semi-circular canals of the internal ear from disturbances of the fluid therein due to head movements and is, therefore, central in origin. Sickness technically termed vertigo can be produced by rotatory movements of the head, apart from disease of the central nervous system.

Symptoms.—These vary from slight giddiness, headache and nausea to violent and projectile vomiting, accompanied by extreme restlessness and later prostration.

Factors influencing causation and severity :

(a) *The subject.*—Some persons are by nature sensitive to all road travelling either in the plains or hills; a vast majority of them are, however, victims of the disease only in the hills. The oversensitive cannot stand even the sight of a vehicle, leave aside actual riding in it, if previous experience of travelling has been unpleasant, and begin to feel nausea immediately. The strong psychic influence can be judged from the fact that I have seen persons who cannot possibly be persuaded to occupy a seat in such an innocuous vehicle as a tonga where speed or sharpness of bends in the road cannot provoke the onset of sickness. Indeed, a sort of 'vehicle-phobia' is developed in them. Others are sensitive to a slight degree only and can generally travel fairly comfortably unless the other factors markedly predominate. All degrees of proclivity to sickness occur between these two extremes. Then again, some persons are better off with empty stomach, others actually comfortable after moderate eating. A full stomach is decidedly disadvantageous and promotes the onset of sickness. The kind of food makes little difference but solids are generally tolerated better than fluids, presumably because of smaller volume. Distension of stomach walls probably excites vagal nerve endings and thus reflexly brings about sickness. Race, nationality, social status and mode of living, sex and age do not influence the causation or intensity of symptoms but habit does. Even those who suffer severely in the beginning get fairly well used to the conditions in due course. Rise in atmospheric temperature during the journey such as is experienced in travelling from a hill station to the plains tends to accentuate sickness in some cases.

(b) *The vehicle.*—The variety of transport does not matter as such and sensitive persons suffer equally whether travelling by train or motor-car—the essential point is the speed of the vehicle. The higher the speed, the worse the symptoms. The position of the seat occupied by the patient is equally important. The

nearer the engine it is, the less the discomfort. Indeed, a person who cannot travel in a back seat at all may be quite comfortable if in the front coach of a train or on the seat adjoining the driver's in a bus. Some are better off just behind the driver of the car on account of repugnance to the smell of petrol fumes. Facing the engine is more comfortable than looking behind or sideways.

(c) *The road.*—Metalled or *kutchha* (unmetalled) road does not make any difference as such though the latter is indirectly helpful because it tends to retard the speed of the vehicle. The important point is the acuity or sharpness and frequency of bends in the road. A straight road even though with marked changes in level due to ravines, hillocks and bridges, does not cause sickness.

After-effects.—Road sickness passes off gradually, depending upon the severity and duration of symptoms and sensitiveness of the individual. A person who has only experienced nausea while travelling may actually vomit shortly after the termination of the journey. There is disinclination to eat for some time but the worst after-effect is the fear of sickness which persists for a long time.

Treatment.—Once actually on, the symptoms of road sickness cannot be relieved unless the operative factors are eliminated. Change of position of the seat and slowing of the vehicle's speed are the main things which can help. Chewing of gum and carminatives like cardamom and anise seeds, sucking of citrate fruits like lemons and orange peels, tamarind seeds and confections such as lemon drops and smoking a cigarette before or during the course of the journey have been tried but seldom prove useful. In some cases a cup of hot tea has soothing effect and relieves the symptoms. Medicines are of no avail either. Sedatives like bromides, chlorotone and even opium do not help to any appreciable extent and are certainly objectionable in view of their after-effects and tendency to habit formation. Efforts to concentrate on other things like reading or conversation with fellow passengers avert the symptoms only temporarily and are not of much use for any length of time. Looking out to breathe free and fresh air is similarly of transitory benefit except when smell of petrol is the chief factor in causation of sickness. Travelling with closed eyes and trying to sleep is of some help as also lying flatly down with eyes shut particularly in the central berth of a train. In short, the sensitive individual's only resort is to persist with courage and try to get accustomed to travelling in conditions which cannot be helped otherwise. Bad travellers can obtain by sheer persistence and practice a fair degree of immunity from road sickness.

Summary.—The causation, influencing factors, symptoms and treatment of road sickness are described on the basis of personal experience.

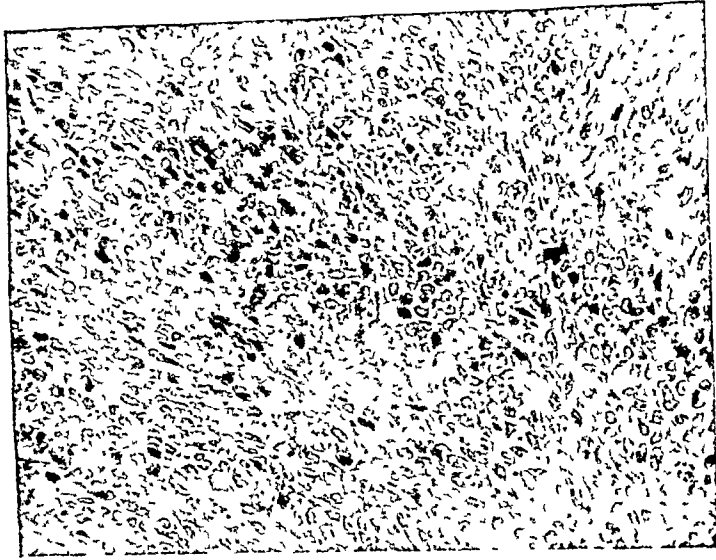


Fig 1

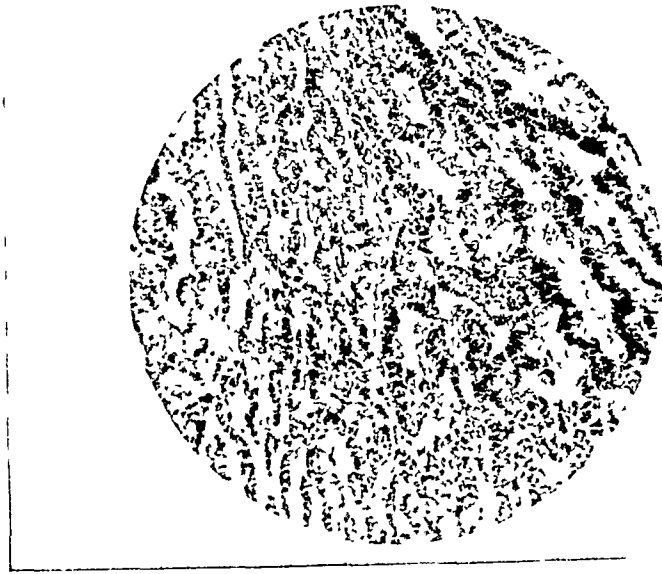


Fig 2

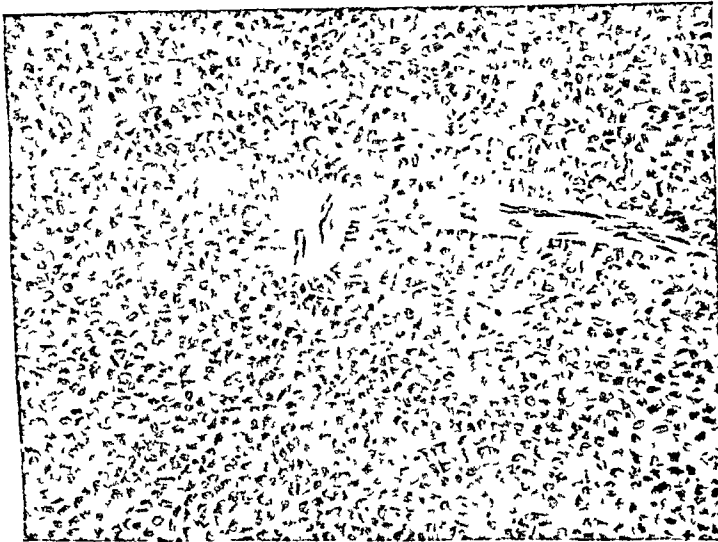


Fig 3

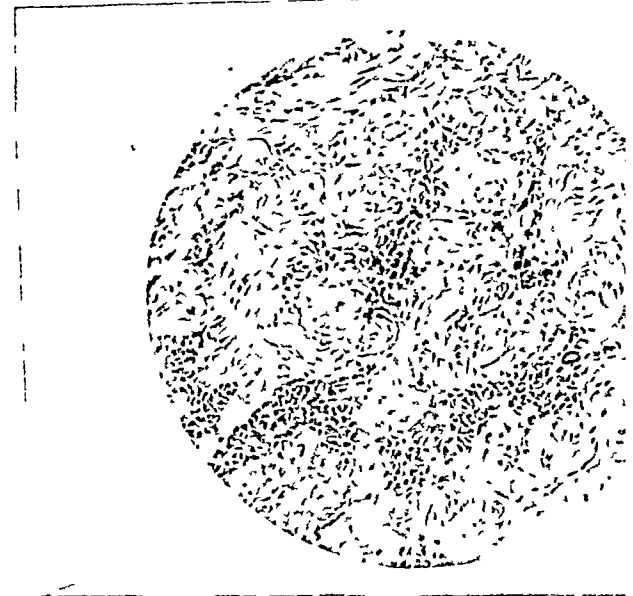


Fig. 4

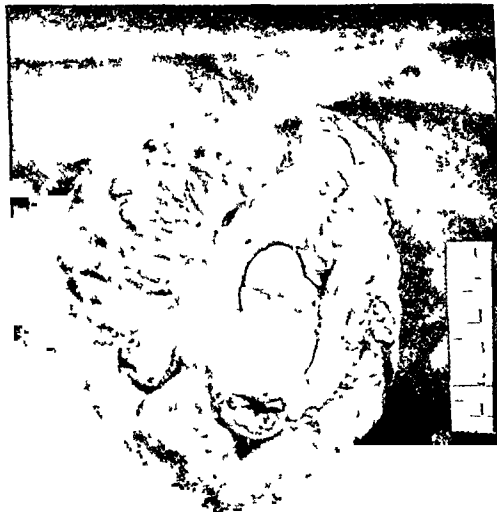


PLATE XXII

A CASE OF POLYMASTIA : K. D. JAIN. (M. H. P.) PAGE 298

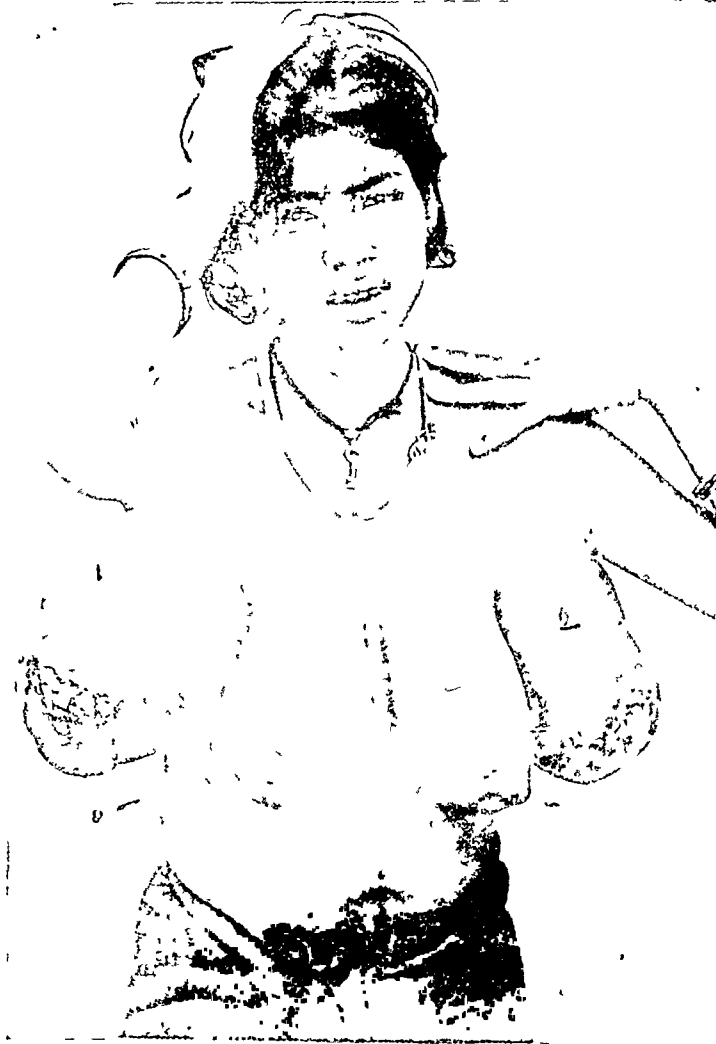


Fig. 1.

A CASE OF RHEUMATIC CHOREA

By K. D. JAIN, M.B., B.S., F.M.S.
U.P. Military Police Hospital, Sitapur

PHUL MATI, aged 6 years, female child, admitted into the hospital with the complaint of inability to walk, and abnormal movements in the whole body for 12 days.

History of present illness.—Twelve days back the child got fever without rigor. It persisted for 3 days. After the subsidence of the fever these movements appeared, first in hands and head, and then over the whole body.

Clinical examination.—Patient is thinly built, temperature 98.6°F., pulse 88 per minute, respiration 18 per minute, tongue slightly coated, throat congested. Movements are involuntary, spread over the whole body, more on the left side. They are mostly irregular and diminished by voluntary action. Sometimes they resemble voluntary movements. They disappear during sleep, get exaggerated when anybody watches them.

Considered regionally: (1) *Upper limbs.*—Movements are mostly in arms pronating and supinating the forearm, flexing and extending the wrists, and rubbing over the eyes and hiding the face like a shy girl when anybody watches the patient.

(2) *Lower limbs.*—Extending and flexing.

Face.—Rolling up of eyeballs, twitching of eyebrow, smacking of tongue and palate, difficulty in swallowing even of liquids.

Tone.—Flabbiness of muscles. Jerk diminished. Plantar response indefinite.

Heart, joints and other systems.—N.A.D.

Blood film.—Apparently leucopænia, no malaria parasites, no abnormality of cells.

Stools.—Nothing abnormal.

Treatment.—Besides giving rest, nutritious diet was given and hyoscine hydrobromide injection daily (gr. 1/100 for five days). The patient was discharged cured after 3 weeks.

Therapeutic Notes

NOTES ON SOME REMEDIES

XXIX.—DEHYDRATION AND ITS TREATMENT,* Part I

By R. N. CHAUDHURI, M.B. (Cal.), M.R.C.P. (Edin.),
T.D.D. (Wales)

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Physiological considerations

WATER constitutes 70 per cent of the body weight. The portion contained within the cells,

* For better understanding of the treatment, the aetiology and symptomatology are first described.

including the blood corpuscles, is known as the intracellular fluid. The rest, known as the extracellular fluid, is contained in blood vessels as plasma and in tissue spaces. The body water may therefore be conveniently described as existing in three compartments; the blood vessels containing plasma; the tissue spaces containing interstitial fluid (including lymph); and the cells containing intracellular fluid (Gamble, 1942). The distribution of water in the different compartments in a man weighing 70 kg. (11 stones) is approximately as follows:—

	Per cent of body weight	Volume (litres)
Intracellular ..	50	35
Extracellular—		
Tissue fluid ..	15	11
Plasma ..	5	3
	—	—
TOTAL ..	70	49
		(11 gallons)

Water passes freely through the cell membrane and capillary wall which divide these compartments one from another, its direction and magnitude being determined by the amount of protein and salts in the various compartments. A dynamic osmotic equilibrium is maintained. There is an interchange of fluids between the gastro-intestinal tract and the blood, between the blood and interstitial fluid, and between the latter and the intracellular fluid. If the plasma volume is reduced, it is promptly restored from the interstitial fluid. The extracellular fluid constitutes what is called the internal environment of the body; it serves to transport nutrient and waste materials and to maintain an approximate constancy in hydrogen-ion concentration and osmotic pressure. It is this fluid which is primarily affected in dehydration.

The body derives its water from beverages, from water contained in foods and from the water of oxidation of proteins, fats and carbohydrates. The average daily water intake in a temperate climate is about 2,600 ml. The output is also the same, consisting of 1,500 ml. in the urine, 600 ml. in perspiration (insensible), 350 ml. in the expired air and 150 ml. in faeces. The amounts lost depend greatly on the environment and on the fluid intake, but it should be noted that even if all water intake stops, the skin and lungs continue closing the usual amount, i.e. nearly 1,000 ml., while the amount excreted by the kidneys is reduced to about 500 ml. The

latter is the minimum urinary volume required for excretion of waste products. This unavoidable loss of 1,500 ml. may be an important factor in the ætiology of dehydration. The water intake and output are greater in the tropics; a man doing muscular work may lose as much as 10 litres of sweat in a day. The body tends to keep its water content at a constant level by variations in the intake in response to thirst, and by variations in the urine volume to counterbalance changes in the water-loss by skin and lungs. Death occurs when the loss of water reaches approximately 15 per cent of body weight or 20 to 22 per cent of body water.

The body's retention and distribution of water mainly depends on salts; in their absence it is not possible to maintain its volume. The extracellular fluid has sodium as the predominant basic ion (90 per cent) and chloride as the main acid ion (70 per cent); plasma differs from the interstitial fluid mainly in its high protein content. The intracellular fluid has a different electrolyte composition; its main ions are potassium cations and phosphate anions. A proper concentration of sodium and chloride ions in the extracellular fluid is the main factor in maintaining its osmotic equilibrium with the fluid in the cells; of these two ions sodium is the most important. If the concentration rises water passes from the cells to the extracellular fluid and if it falls, a reverse movement of water takes place. Another function of sodium and chloride is that they play principal parts in the acid-base balance of the extracellular fluid. One of the important functions of the kidney is to regulate the volume and composition of the extracellular fluid.

Sodium chloride is then the principal salt which the body requires. An adult needs 5 gm. a day, but it should be higher in hot climate. Any excess of salt above requirements is excreted mostly by way of urine. We get our salt from food and what is added during cooking and taken as a condiment. The total salt content of the body is about 1/400 of the body weight or about 6 oz. in a 70 kg. man, two-thirds of which are in plasma and tissue fluid, and nearly all the rest in alimentary secretions, sweat and urine. The body economizes salt more efficiently than water, for if no salt is taken, the kidneys practically stop excreting salt as soon as the plasma level falls below normal. But if in addition to the stoppage of salt intake there is abnormal loss of sodium chloride by vomiting, etc., a state of hypochloræmia develops.

General causes of dehydration.—Dehydration refers to depletion of water and salt and is caused by excessive loss of body fluids without adequate intake of food, chloride and water to make up for the loss. If a person does not take fluids, he may lose considerable amounts of water through the lungs and skin, even

though its excretion in the urine is reduced. The losses are increased if sweating is profuse as at high environmental temperature (e.g. heat cramps, heat exhaustion) or if the respiration rate is rapid as in acute febrile diseases like pneumonia. Patients sometimes refuse to take water or other drink, may be too weak to ask for it, or may not be given any at all if in states of coma. After operation a patient may lose fluid through sweat which is promoted by extra blankets or hot water bottles. More serious dehydration occurs from persistent vomiting and acute or chronic diarrhoea. In acute poisoning with violent vomiting and diarrhoea serious salt and water deficiency may develop—a fact which is apt to be forgotten in treatment. A rare but important cause is gastric or intestinal suction drainage, in itself a valuable method of treatment, which can cause withdrawal of a large amount of sodium and chloride ions. In Addison's disease there is failure of the cortical hormone of the suprarenal gland causing excessive secretion of sodium chloride and water in the urine. Shock is often associated with dehydration.

Clinical manifestations.—It is now recognized that dehydration may arise from primary loss of water or be secondary to a reduction in the salt content of the body. Although in clinical practice the two conditions are often more or less combined, it is important to know which deficiency is predominant, as the mechanism of production and treatment differ in each case.

Water deficiency

This occurs from inability to swallow or obtain food and water owing to great weakness, coma or other causes. Ship-wrecked men in boats and men lost in desert suffer from this kind of deficiency. Starvation is a well-known cause. Water is lost through the lungs, skin and urine, but there is no significant loss of sodium chloride. The extracellular fluid therefore becomes hypertonic, but tends to maintain itself by withdrawing water from the cells. Because of this cellular desiccation thirst is pronounced; the voice is husky and dryness of mouth makes swallowing difficult. The patient looks ill and has a peculiar pinched appearance of the face. The urine is concentrated, low in volume with a specific gravity above 1030 and has sodium chloride in it. Although weakness is progressive, the circulation is well maintained and there is no reduction of blood volume and no renal failure until late, when mental power becomes impaired and there may be confusion and hallucinations. The patient retains the power of absorbing water and may recover rapidly after water ingestion. In this form of deficiency the water loss is twice as much from the intracellular as from the extracellular fluid (Black, 1945).

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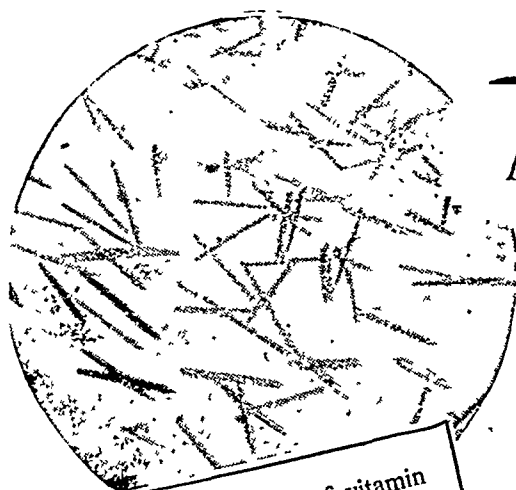
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Indian Medical Gazette

JULY

THE PEN

THE act of writing expresses the individuality of the writer as the act of speaking expresses the individuality of the speaker. As a matter of fact writing is much more expressive than speaking.

The commencement of a word, rate of delivery and accentuation of syllables in its continued articulation, and its termination are essentially individualistic, apart from other general distinguishing qualities in voice, such as piping, grating, drawl or huskiness. In writing, the individuality goes further and affects letters instead of words. The commencement of a letter, shaping of its major portion in a graph of varying thickness and its ending are comparable to the syllables of a word. One begins with a deliberate pressure, sustains the pressure at a varying level and relieves the pressure at the end. In doing so one makes characteristically bold, meek or nondescript beginning, elegant or utility curves varying in thickness, later, and equally bold, meek or nondescript ending. All these steps make the pattern which the handwriting expert recognizes at a glance. The pattern is characteristic like the posture and gait of an individual possessed of a normal nervous system and free from diseases of bones and muscles.

The pattern is made best by the smooth writing point of a nib initially and a yielding preceding part later. In a quill, that most perfect of writing devices, the smooth point and the yielding preceding part are at their best, provided a good quill cutter is available. Alas, he disappeared over a decade ago! The last of his line could not be traced in Messrs. Thacker, Spink & Co. of books and stationery fame several years before the World War II. He was ousted by the manufacturers of fountain pens.

The fountain pens made for the last generation competed with the quill well: that is how they ousted it and its cutters. They had nibs which were smooth at the points and flexible in the preceding part. They commenced writing at once and by bending before the fingers responded to the will of the writer. Thought flowed through them smoothly, swiftly and uninterruptedly.

Smoothness leads to smoothness, more smoothness and yet more smoothness, reciprocally on the paper and in the brain. The romance writers of the days of the quill have left behind them characters and scenes in pen pictures that the sensation mongers of to-day will never be able to copy even badly. The modern romances are mostly tales 'full of sound and fury and

signifying nothing'. The old writers wrote, the present ones type or dictate. They lack the expression ripened in the cerebrum through smoothness reacting on smoothness in writing.

Goods to-day are sold by creating demand, not by studying and meeting demand. The expensive fountain pens are so palmed upon millions of scribblers. Advertisement costs more than the manufacture. Elegant shapes inlaid and overlaid with metal supposed to be precious, descriptions of silken smoothness of writing, mention in terms of mechanics—applicable really to buildings, canals, engines and guns—of devices which ensure an easy flow of ink, and some quite commonplace figure on the clip or the cap make one remember them. The dealers remind one further. The pens are bought at fancy prices. They are useless if not actually harmful. Their rigid nibs instead of following the fingers make the fingers follow them. Result: Frustration. One wonders if the psychoses, born of frustration, in the educated young men to-day are not produced by pens with rigid nibs alone. Not being able to put down on paper, in their own way, their lecture notes and later their answers to questions, they pass their examinations in the lowest division and fail to find jobs. For lack of expression they fail to tell others what they want or what worries them, run amok, throw things to injure inoffensive fellow citizens, and burn buses and tramcars.

The old-fashioned fountain pens planned before the World War I are still in existence. Let the reader try them. They are easy to recognize by a fairly large nib and its flexibility. The nib is made of gold which resists corrosion and the point is covered with iridium which resists wearing. Most of what was good in quills is to be found in these pens. The nibs of cheap pens available in Disposal Shops (from stock meant for G.I.'s of the U.S.A.) were of a yellow metal which appears to be as good as gold in yielding to the fingers and not yielding to corrosion. The point may not be as durable as the one covered with iridium. The metal may with advantage supply nibs for cheap pens. The worn out nibs could be changed after a few years at the cost of a rupee or so.

Incidentally, the makers of most of the most boosted new pens with rigid nibs use very little gold. The tiny gold nib they hide under a 'hood' to 'protect it from dust and dirt'. Yet, some of them convert the entire lower end of the pen into a tubular nib which is exposed to dust and dirt all round and on two surfaces, external and internal. Evidently the protection supplied to the expensive pen number one is not necessary for the expensive pen number two. Really it is not necessary at all. The hood is meant for the customer.

Then there are atrocities inflicted as pens writing with a ball bearing point. They are worse than pencils points of which after a few

seconds of writing do adjust themselves to one's fingers and pressure.

Medical men whose handwriting is known to be rather difficult to read will do well not to worsen it by using defective though expensive pens which their grateful patients might give them as presents. With the ball bearers they should have nothing to do although some of them are advertised in the medical press.

A problem needing special attention is the use of fountain pens by school children. They are losing individuality in caligraphy. With pens with rigid nibs all children write alike, more or less; as all paraplegics, tabetics or cases of paralysis agitans walk alike, more or less. Such pens in particular and fountain pens in general should be forbidden in schools. They thwart, dwarf and paralyse personality.

Special Article

DIAGNOSTIC METHODS IN DISEASES OF THE LIVER

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RECENT studies of intrahepatic diseases have shown that serious lesions of the liver may arise not only from the presence of noxious substances but also from the deficiency of essential nutriment. In order to foresee the future course of the disease and institute adequate therapeutic measures in such cases, the clinician wants to learn more than just the presence of hepatic damage; he wants to know the anatomic form of the lesion and the extent to which it has progressed. Until recently, this expectation has only been partially fulfilled. Although numerous tests of liver function have been devised, these have only proved useful in so far as indicating the presence and degree of hepatic damage, and following its progress, rather than the means of accurate lesion diagnosis.

Wahi and Chakravarti (1946) and Hoffbauer *et al.* (1945) in correlative studies of the clinical, chemical and histological findings, showed the difficulties in the interpretation of liver function tests in the light of histological findings and concluded that the cause of the liver damage in most cases can be established by biopsy studies alone. It was further shown that a combined study of the liver functions and the histological findings in the biopsy specimens provided a more definite information about the nature and extent of the underlying lesion.

Furthermore, in the development of alcoholic and other nutritional types of cirrhosis (diffuse

hepatic fibrosis of Himsworth, 1947), there is an initial reversible change characterized chiefly by fatty infiltration, which is later followed by an irreversible change characterized chiefly by increasing fibrosis. The amount of fibrous tissue in the liver may be used to estimate the extent of damage and hence the prognosis in cases of cirrhosis. Since, neither liver function tests nor histological studies gauge accurately the extent of damage or fibrosis of the liver, quantitative estimation of fibrous tissue in cirrhotic livers would give a correct index to the degree of permanent damage to the liver (Warren and Wahi, 1947).

For a complete evaluation of a diseased liver, a combined study with function tests, puncture biopsy, and estimation of fibrous tissue in cirrhotic livers would thus be most informative. The utility and limitations of these diagnostic procedures will be considered below in light of experience gained by the studies carried out at the laboratories of Pathology of the Agra Medical College and the New England Deaconess Hospital, Boston.

Liver function tests

The liver is a composite organ with multiple functions, and as such, several or all of these functions may be disturbed by hepatic disease. Broadly speaking, the tests of liver function fall into three categories depending upon the function disturbed—tests of excretory function, tests of ability to synthesize, and certain empirical tests for liver damage. The function disturbed depends upon the type and the stage of the disease, and may vary in different patients in the same stage of the same disease. It is comprehensible because in this complex organ, there are in addition to the vascular and supporting structures three other well-differentiated tissues with highly specialized functions: the parenchyma, the cells of the biliary tract and the reticulo-endothelial system represented by Kupffer cells. The composite nature of the organ as a whole is preserved even in the smallest anatomical unit, the lobule. Consequently, injury to any part of the liver commonly involves contiguous though distinct tissues, and the symptomatology of any hepatic damage is thus the end-result of disturbed functions of these different tissues. It is thus obvious that no single test can be expected to give adequate information concerning the underlying pathology.

For purposes of clinical analysis, the symptomatology of hepatic failure can be separated into three syndromes—excretory failure, parenchymal failure and portal obstruction. However, the patient usually presents a complex picture comprising of more than one syndrome. It is necessary, therefore, to employ a group of tests in any suspected case. This is all the more essential in early or mild cases where only one of the many tests may be positive. Besides,

individual tests used for determination of hepatic dysfunction are also affected by certain extra-hepatic conditions, *i.e.* cephalin-cholesterol flocculation in malaria and infectious mononucleosis; proteins in nephrosis and nephrotic syndrome; phosphatase in bone diseases; bilirubin and urobilinogen in hæmolytic process; cholesterol in thyroid affections, diabetes, nephrosis and other diseases. Further, the tests should be repeated frequently because at some stage of certain acute hepatic diseases these may show variations, being positive one day and negative the next, without any accompanying clinical changes in the patient.

Hepatic function tests are not specific for any particular type of disease nor do they indicate a primary or secondary involvement of the liver. Their diagnostic value depends upon their being interpreted in the light of available clinical findings, the course of the disease and results of other diagnostic procedures. Other pathological entities likely to influence the results should also be excluded. However, if properly selected, performed and interpreted, the hepatic tests should greatly assist in diagnosis and following the progress of the case.

Three main situations which arise for application of liver function tests are :

- (1) Diagnosis of acute infectious hepatitis and its sequelæ.
- (2) Differential diagnosis between hepatic, extrahepatic obstructive, and hæmolytic jaundice.
- (3) Diagnosis of and following the therapy in hepatic cirrhosis.

Diagnosis of acute infectious hepatitis and its sequelæ

The tests likely to prove of value are :

- (a) Bromsulphalein excretion test.
- (b) Thymol turbidity test.
- (c) Serum and urine bilirubin determination.

The most important feature of the laboratory diagnosis of infectious hepatitis is that the value of different procedures varies with the stage of the disease. This is well illustrated by bilirubinuria, one of the dependable tests early in the disease, but of no value later on because of an apparent increase in the renal threshold to bilirubin. Further, in the absence of fever, results of liver function tests have increased significance.

Bromsulphalein excretion test.—This is one of the most sensitive indicators of mild hepatic damage and is particularly useful for the detection of hepatic dysfunction not usually manifested by jaundice. It is indicated in all patients with suspected liver disease who do not have obvious jaundice, since marked bromsulphalein retention in the absence of icterus is particularly pathognomonic of intrahepatic disease. In infectious hepatitis the test becomes positive in pre-icteric stage and remains positive during the period symptoms are present.

As liver derangement and obstruction of the biliary passages both interfere with the excretion of bromsulphalein, the test is of no value in differential diagnosis of jaundice.

The test is also positive in active portal cirrhosis as well as in most of the other conditions associated with focal or diffuse hepatic injury. It is probably the best single test for chronic hepatitis. The positive results are, however, not specific for primary liver disease, as the test is sometimes positive in non-specific conditions like malaria, pneumonia, cardiac failure and infectious mononucleosis (Lichtman, 1942; Lippincott *et al.*, 1945; Bockus *et al.*, 1946; Cohn and Lidman, 1945). Repeated determinations are useful as an index of progress especially in non-icteric hepatic diseases.

Bromsulphalein retention between 5 and 10 per cent after 45 minutes should be regarded as suspicious. Retention greater than 10 per cent after 30 minutes and 6 per cent after 45 minutes is definitely abnormal (Neefe *et al.*, 1944; Mateer *et al.*, 1943; Neefe, 1946a, 1946b; Israel and Reinhold, 1938).

Thymol test.—This test recommended by MacLagan (1944a, 1944b) is based on the reaction between thymol and qualitatively or quantitatively altered serum globulins. It is better to use the name 'thymol test' for the combined procedure of turbidity as well as flocculation. Originally, MacLagan did not include observation for flocculation as a part of the test, but recently Neefe (1946a) has shown that in certain stages of chronic hepatitis significant flocculation occurs with otherwise normal readings for turbidity test.

The thymol test is usually positive in infectious hepatitis, homologous serum hepatitis, and active portal cirrhosis (MacLagan, 1944a, 1944b; Neefe, 1946a, 1946b; Watson and Rappaport, 1945). In infectious hepatitis, it is a delayed rise usually coming after the symptoms are gone and probably follows healing. At certain stages of chronic infectious hepatitis without jaundice, the thymol test may be the only means of finding the persistence of the lesion and Neefe (1946a) reported that only flocculation may be present without turbidity in these cases.

Like the cephalin-cholesterol flocculation and colloidal gold tests, its general significance seems to be that a positive reaction indicates active damage occurring in the parenchyma (Maizels, 1946; MacLagan, 1944a, 1944b) while in cases of uncomplicated extrahepatic obstructive jaundice it is usually negative. A negative test, however, does not exclude intrahepatic jaundice and sometimes cephalin-cholesterol flocculation test may give positive results in such cases (Neefe, 1946a, 1946b) or it may be *vice versa*. Thus it is imperative to employ, if possible, both the tests to rule out hepatic damage. Positive results have also been reported in rheumatoid arthritis, heart failure, pernicious anæmia,

The greatest increase in serum alkaline phosphatase occurs in obstructive jaundice, though also present in smaller degree in parenchymatous liver disease. Deep jaundice due to biliary obstruction is associated with marked elevations of alkaline phosphatase, whereas deep parenchymatous jaundice may or may not be associated with higher values. However, if hepatocellular damage is associated with intrahepatic obstruction, high values for alkaline phosphatase are usually encountered (Hanger and Gutman, 1940). It would therefore seem that a negative finding, suggesting a hepatic rather than obstructive cause of jaundice, is more useful than a positive result in differential diagnosis of jaundice. Other conditions like diseases of the bones which give rise to increased serum alkaline phosphatase must be excluded before interpreting the results.

With the methods of Bodansky (1933) and Shinowara *et al.* (1942) values greater than 4 to 8 units are regarded as abnormal for adults. 75 per cent of patients with obstructive jaundice have serum alkaline phosphatase greater than 25 units per 100 cc. Mawson (1948) reported that in his series all cases with phosphatase greater than 40 units per 100 cc. were obstructive jaundice, and all with phosphatase less than 17 units per 100 cc. were infective hepatitis.

Serum lipoids.—Total serum cholesterol and cholesterol esters.

Cholesterol metabolism is connected with liver, and more intimately so is the amount of serum cholesterol esters. The total and esterified cholesterol are both influenced by liver disease, the latter more especially. Hence the percentage of total cholesterol that is in the esterified form is used as an index of liver function (Epstein and Greenspan, 1936; Chanutin and Ludewig, 1936; Epstein, 1937; Greene *et al.*, 1940; Thannhauser and Schaber, 1926). Serum lipid determination is therefore used as an aid in the differential diagnosis between obstructive and parenchymatous jaundice, as well as a prognostic guide in chronic liver diseases.

In uncomplicated obstructive jaundice, the total cholesterol is usually increased proportional to the degree of obstruction, while the percentage of cholesterol esters may be normal or decreased though their marked decrease is usually associated with a concomitant liver damage (Epstein and Greenspan, 1936).

In hepatocellular jaundice, there is a decrease in the percentage of esterified cholesterol, the extent of which is roughly parallel to the degree of the liver damage. Total cholesterol may also be decreased in more severe cases but this is more relative than real as it seems to be due to the result of decrease in esters.

In certain instances results of cholesterol determination may overlap and the interpreta-

tion may thus become confusing, i.e. in partial obstruction of the biliary passages, in mild hepatocellular jaundice, and in certain cases of intrahepatic obstructive jaundice. In the healing stages of hepatitis, the total cholesterol may be increased considerably, with esters remaining normal. On the other hand, in partial obstruction of biliary passages, the total cholesterol may show no significant rise. This shows the inadvisability of basing the diagnosis of hepatic damage on single tests.

Serial determinations of serum cholesterol may be of help in gauging the prognosis in cases of hepatic damage. Constant and persistent decrease in total cholesterol and a persistent decrease or absence of cholesterol esters is of grave prognostic omen. On the other hand, increase in the percentage of cholesterol esters is suggestive of improvement. Normally 50 to 65 per cent or 70 to 75 per cent of total cholesterol is, in the esterified form, depending upon the method used.

Group B.—The thymol test and its interpretations have already been discussed. Positive thymol turbidity in cases of jaundice indicates hepatocellular damage, as an uncomplicated obstructive jaundice gives negative results. Mawson (1948) found in his series that all cases with thymol turbidities less than 2.2 units combined with phosphatases higher than 31 units per 100 cc. had obstructive jaundice.

Cephalin-cholesterol flocculation test

This test was originally proposed by Hanger (1938, 1939) based on his observations that serum from patients with certain hepatic diseases caused flocculation of cephalin-cholesterol emulsion, while serums of normal persons and from patients with uncomplicated obstructive jaundice did not produce flocculation. Kabat *et al.* (1943) and Moore *et al.* (1945) have suggested, from their studies of the mechanism of the test, that flocculation reaction is dependent on the changes in the albumin and gamma globulin fractions of the serum proteins, particularly in cases associated with active parenchymal damage. Gamma globulin derived from normal human serum produces flocculation of cephalin-cholesterol emulsion, while a mixture of albumin (from normal human serum) and normal gamma globulin produces no flocculation. Apparently, the normal human serum albumin inhibits the flocculation reaction. However, the albumin derived from the serum of patients with infectious hepatitis does not inhibit this reaction, and the cephalin-cholesterol flocculation reaction is positive. The same mechanism is probably true in cases of other hepatic diseases associated with active damage to the liver cells. Cephalin-cholesterol flocculation reaction therefore depends upon a balance between flocculation effect of gamma globulin and the inhibiting effect of the albumin fraction.

Positive reactions strongly suggest the presence of active hepatic disturbances, probably parenchymal in nature (Neeffe *et al.*, 1944; Hanger, 1939; Hanger and Patek, 1941; Nadler and Butler, 1942; Pohle and Stewart, 1941; Rosenberg and Soskin, 1941). In infectious hepatitis and homologous serum jaundice the test is positive in the pre-icteric stage and remains positive through the jaundice period. It may or may not become negative during the recovery stage. It is also frequently positive in cases of hepatitis without jaundice, active, portal and biliary cirrhosis and other diseases associated with injury or necrosis of the liver cells. The reaction is negative in uncomplicated obstructive jaundice (Rennie and Rae, 1947), and therein lies its value in the differential diagnosis of medical and surgical jaundice, especially early in the disease when complications like secondary liver damage or infections which may give positive reaction are absent.

It must however be reckoned that the test is not specific for primary hepatic damage, as positive results are also reported in certain diseases where the hepatic involvement, if at all, must be secondary, *i.e.* malaria, pneumonia, septicæmia, infectious mononucleosis, amœbic hepatitis and thyrotoxicosis (Lippincott *et al.*, 1945; Guttman *et al.*, 1945; Kabat *et al.*, 1943; Moore *et al.*, 1945; Mawson, 1948). On the other hand, persistently negative results do not exclude hepatic involvement, *i.e.* cases of metastatic malignancy and hepatitis not associated with active injury of the hepatic cells (Hanger and Gutman, 1940). In some of these cases thymol test is positive, while cephalin flocculation test is negative, and hence the necessity of performing the two tests simultaneously.

Repeated tests during the course of the disease may offer evidence of considerable prognostic value. A change from negative to positive would suggest onset of cellular damage, while a change from positive to negative would suggest decreased activity. Persistently positive results during the course of hepatitis mean continued activity.

Readings of 1+ or more at 2 hours and 2+ or more at 48 hours are regarded as abnormal. 1 to 2+ after 48 hours are considered as suspicious.

Determination of serum gamma globulin

The intimate association of the liver with the maintenance of normal serum protein is well accepted. Hepatic diseases may characteristically result in alteration of the serum proteins, *i.e.* decrease in serum albumin and increase in serum globulin with inversion of the albumin-globulin ratio, as well as decrease in fibrogen and prothrombin (Post and Patek, 1943; Loeb, 1941; Madden and Whipple, 1940; Brinkhous, 1940; Myers and Keefer, 1935; Gray, 1942; Tumen and Bockus, 1937). The usual chemical

determination of serum proteins has led to the conception that proteins may be considered normal when the serum albumin and globulin content falls within normal range. By electrophoretic analysis, however, the protein fractions within the serum globulin (alpha, beta and gamma) may be markedly abnormal, although quantitatively the globulin may be within normal range. Luetscher (1940) and Longworth *et al.* (1939) showed by electrophoretic studies that an increase in beta and gamma globulin, associated with a decrease in albumin, occurs in cirrhosis of the liver. Gray and Barron (1943) made electrophoretic analysis of serum proteins of patients with different types of liver diseases. They found that the most consistent and characteristic protein abnormality in liver disease is the increase in the largest molecular weight fraction, the gamma globulin, and the impaired production of the smallest molecular weight protein, the albumin. These changes are seen most frequently and in the greatest degree in cirrhosis of the liver and acute parenchymatous diseases.

Jaundice alone does not produce significant alteration of serum proteins. Although serum albumin may be decreased in some cases, the gamma globulin is essentially normal in extra-hepatic jaundice. Herein lies the value of gamma globulin determination in differential diagnosis of medical and surgical jaundice. It must, however, be remembered that prolonged jaundice alone may cause early liver damage, and increased gamma globulin values in clinically uncomplicated jaundice may reflect these changes.

Tests useful in diagnosis of, and for evaluation of therapy in hepatic cirrhosis

(a) Serum protein determinations, specially serum albumin and gamma globulin levels.

(b) Bromsulphalein retention.

Serum protein determination.—One of the most important functions of the liver cell is protein synthesis, and a persistently low level of plasma albumin in a patient who has had signs of liver disease is a sufficient proof of the failure of one of the synthetic functions of the liver, provided food intake is adequate and gross albuminuria is absent.

The most consistent and characteristic abnormality is hypoalbuminæmia, associated with increased serum globulin. These changes are seen most frequently and to the greatest extent in cirrhosis of the liver and next most frequently in acute parenchymatous diseases. In extra-hepatic jaundice the globulin values are normal.

Post and Patek (1943) have produced data to show that changes in the level of the serum albumin have a good correlation with the clinical course of hepatic cirrhosis. In patients who improve and remain in good health, the serum albumin rises to normal values and remains

there. In those patients who show temporary improvement, serum values go up but never reach the normal levels. The prognosis has to be guarded in these cases in spite of their periods of clinical improvement. These cases who run a downhill course have a constantly low figure, which may even show a gradual decline. Furthermore, accumulation of fluid in ascites may also be correlated with serum albumin levels, though hypoalbuminæmia mostly acts in conjunction with portal hypertension, the latter primarily deciding the localization of the fluid to the peritoneal cavity. If ascitis occurs in the presence of normal serum albumin, one should look for an extrahepatic cause, *e.g.* portal vein thrombosis, malignancy, etc., as a contributory factor.

Serum total proteins and serum globulin do not reveal any significant differences between the patients who improve and who die (Post and Patek, 1943). However, if there is a concomitant elevation of the plasma globulin level associated with hypoalbuminæmia, then the subnormal level of plasma albumin has probably been present for a considerable time, and indicates the chronicity of the process and poor prognosis from the point of view of curability. The disease usually then follows a swiftly downhill course.

The significance of this protein abnormality in liver disease will however depend upon the exclusion of other conditions which might be responsible for hypoalbuminæmia, besides impaired synthesis by liver, *e.g.* protein starvation or extensive utilization. Patients with starvation hypoalbuminæmia differ from the cirrhotics in that elevated serum globulin which is so common in cirrhosis does not occur in the former. In protein deprivation, the total serum proteins are low and almost always at the expense of serum albumin. Another important point of difference is the rapidity (10 to 20 days) with which low serum albumin due to starvation can be restored by feeding the patients with one or two grammes of proteins per kilogram of body weight per day, while the cirrhotics do not show such prompt improvement (Post and Patek, 1943). This is due to the fact that after prolonged low protein feeding, histological and functional changes occur in the liver (Weech and Goettsch, 1938; Elman and Heifetz, 1941; Himsforth, 1947; Wahi, 1949). These changes may be part of the impaired function of the liver leading to faulty albumin synthesis (Post and Patek, 1943). Serial serum albumin determinations would thus be useful in indicating the response to high protein diets in cases of cirrhosis of the liver. If the albumin level goes up, it would mean that the hepatocellular injury is not far advanced to interfere with the synthetic function of the liver cell and the patient has a good prognostic outlook.

Bromsulphalein retention.—It is the most important single test of hepatic function for

following the progress of alcoholic cirrhosis. Tumen and Bockus (1937), after comparing the serum protein levels with bromsulphalein test, came to the conclusion that the dye test occupies a somewhat superior place in the diagnosis of cirrhosis without jaundice, since extrahepatic causes may occasionally produce hypoalbuminæmia, whereas marked bromsulphalein retention in the absence of jaundice is practically pathognomonic of intrahepatic disease.

Other tests besides the above have also been advocated for judging liver function. The hippuric acid synthesis is a useful test, provided it is done carefully, and kidney damage is excluded, as normal excretion of hippuric acid is essential for correctly assessing the result. Cases have been reported, however, where liver and kidney functions were demonstrated as normal and yet the test gave low figures (Wahi, 1946; Sherlock, 1946).

Prothrombin response to vitamin K has also been advocated as a test of liver function, especially for differentiating obstructive from hepatocellular jaundice (Wahi, 1947; Lord and Andrus, 1941). The test, however, cannot be frequently performed for this purpose as the initial prothrombin levels may be normal in both types of jaundice. Also in cases of obstructive jaundice with secondary liver damage the prothrombin response may be absent or delayed.

Puncture biopsy of the liver

From the above consideration of the liver function tests it is obvious that at best, even when the entire battery of such studies is employed, the information obtained is, most of the time, imperfect. These have proved useful in detecting the presence and the degree of functional damage and for following the progress of the intrahepatic disease, but have failed to give the indication as to the anatomical diagnosis. This information is essential to formulate the future course of the disease. Therein lies the value of obtaining exact histological information by means of needle biopsy. For some time now, we have been interested at the Thomason Hospital, Agra, in the histopathological studies of the liver diseases (Wahi, 1946a; Wahi and Chakravarti, 1946; Wahi and Mathur, 1947), and have found, as others have (Iverson and Roholm, 1943; Sherlock, 1945; Hoffbauer *et al.*, 1945; Volwiler and Jones, 1947; Himsforth, 1947), that such knowledge is frequently vital in making a precise clinical diagnosis to institute the specific therapeutic regimen, evaluate the results, and advise the patient regarding the prognosis. In other words, such information is absolutely necessary for effective handling of the patient.

In spite of the obvious usefulness of this procedure as a diagnostic method, it has not been universally adopted owing to the controversy regarding its slight but undeniable risk of hæmorrhage from perforation in the liver, and

adequacy of the material so obtained for histological examination. Taking an overall view, which is after all the reasonable attitude to adopt towards any diagnostic procedure, the advantages of its use in careful hands outweigh its dangers. There are two methods at present for obtaining biopsy specimens, laparotomy with a small incision under local anaesthesia and needle biopsy. Laparotomy is discomfiting and unnecessarily alarming to the patient, who considers this as a major operation. It is not justified if the other method is available. If visual help is considered necessary, it is advisable to use peritoneoscopy, as the area visualized is considerably greater than the one seen through the laparotomy incision. However, even this is a painful procedure and the patients do not agree for repeated biopsies to follow the course of the disease. Besides, in chronic diffuse hepatitis an adequate sample of tissue may not be obtained, and one may only get a portion of the thickened liver capsule. However, peritoneoscopic biopsy has certain definite uses, especially when looking for a focal lesion, *e.g.* primary tumour or a metastatic nodule. This procedure is useful in gross visualization of the liver in diffuse hepatic lesions and helps in dealing with the site if bleeding is profuse.

Considering the discomfort, expense, prolonged preparation and constant use of the operation theatre in these two procedures, the third method, *e.g.* puncture biopsy, is the method of choice. It can be performed at the bedside and, when properly performed, causes little discomfort and usually provides a fairly satisfactory sample of tissue. The development of this technique has already been discussed (Wahi, 1946a). The writer has found the Vim-Silverman needle satisfactory but is as satisfactory as the others (Volviler and Jones, 1947; Gillman and Gillman, 1945; Dible *et al.*, 1943) in skilled hands. However, it has its dangers and limitations. Its main drawback is haemorrhage from perforation in the liver, and the puncture biopsy should never be done on any patient who is either bleeding or whose prothrombin concentration is subnormal. In those cases where the elevated prothrombin time has been resistant to parenterally administered vitamin K, an effort might be made to reduce the same temporarily by a freshly drawn, citrated whole blood transfusion just prior to biopsy. Owing to same reasons chronic venous congestion of the liver has been considered as a contra-indication to needle biopsy by some workers, although we have obtained, without untoward accident, biopsy specimens in twelve cases, and Sherlock (1945) and Volviler and Jones (1947), 25 and 4 cases respectively. Failure to secure specimen usually occurs when the organ is fibrotic, the specimen consisting then of only parenchyma, or when the lesion is localized as in metastatic nodules, or when ascitis is present even though paracentesis is performed pre-operatively.

By puncture biopsy of the liver the writer (Wahi, 1946a) has diagnosed diseases clinically unsuspected, including amyloidosis, miliary tuberculosis, reticulo-endotheliosis, carcinoma and portal cirrhosis. It has been valuable in changing the clinical diagnosis and the adapted course of treatment. Cases treated for amebic hepatitis turned out to be chronic diffuse hepatitis, while some labelled as endemic ascitis proved histologically to be portal cirrhosis. A case diagnosed and treated as kala-azar turned out to be cirrhosis of the liver. Thus biopsy may provide the only reliable information regarding the kind of intrahepatic disease present, and when laboratory function tests are completely normal, biopsy alone will give a clue to the aetiology of hepatic enlargement.

The differentiation of intrahepatic and extrahepatic obstructive jaundice poses one of the most important and difficult problems for diagnosis to the clinician, who has to decide between surgical and medical treatment. Clinical data and liver function tests may be inconclusive. He has to choose one of the three alternatives—exploratory laparotomy, further observation till the disease becomes obvious and the liver puncture biopsy. The first alternative is usually avoided, for most of the time patients do not agree and also that it may flare up any intra-abdominal inflammatory condition. Decision is usually imperative and urgent and as such prolonged hospitalization for purposes of observation is not a welcome procedure. Besides, it is never certain if the diagnosis will become clear by waiting. By means of puncture biopsy, the diagnosis can often be made early in the disease and the clinician is saved time that is therapeutically valuable to the patient.

With the recently established use of lipotropic substances in the treatment of cirrhosis, it is necessary to diagnose cases in the pre-cirrhotic fatty infiltration stage. Clinical findings and the liver function tests cannot be depended upon for correct appraisal of the disease process, as identical findings may be seen in patients showing histologically marked differences in degree of cellular reaction, cell necrosis, fatty infiltration, reactive fibrosis, and parenchymal regeneration. Obviously much can be expected from the correct and strenuous therapy if instituted at a stage when liver histologically shows an active reparative regeneration usually observed in acute alcoholic fatty livers in temperate climates and nutritional fatty livers in the tropics. On the other hand, disappointing results can be predicted in cases where fibrosis is advanced enough to lead to a stationary histologic picture. Clinically, the seriousness of these cases is usually not obvious until the last stages, and if this is depended upon to impress the alcoholics about the necessity of moderation and following the appropriate therapy much success may not be achieved. Similar is the case with the malnourished people in the tropics,

where the economic conditions prevent them from seeking medical advice till they are acutely ill. Puncture biopsy, by providing an early appreciation of the disease process, may definitely influence the patients in taking treatment while the disease is still curable. Furthermore, biopsy material is sometimes absolutely essential for correctly gauging the results of a therapeutic programme (Volwiler and Jones, 1947). It is not uncommonly experienced that during the treatment of a hepatic disease, serial laboratory examinations show an unchanged poor liver function though the patient looks clinically improved. In such cases, a satisfactory decision regarding when to mobilize the patient and cease stringent treatment may be obtained by biopsy examination. On the other hand, cases of infectious hepatitis may show clinical recovery at a time when liver is still the seat of pathological process. Patients allowed to resume their normal activity at this stage have times out of number sought re-admission to the hospital from exacerbation of their acute illness. Again, liver studies would be the only satisfactory means of correctly evaluating the patient's condition and to impress upon the patient as well as the physician to prolong the precautionary treatment.

The study of liver histology is also desirable before considering the surgical approach to the treatment of portal hypertension by venous anastomosis, as the presence of degenerative changes in the liver cells increases the operative risk, and, in case the operative treatment is decided upon, a long pre-operative dietary regimen will be essential.

In the writer's experience, needle puncture biopsy of the liver has been a satisfactory diagnostic method in diffuse liver disease and necessary sample has always been obtained. The reported mortality rate is only 0.5 per cent. With care, skill and correct judgment, the risk can be further reduced. It is believed that the value of the histologic information obtained by needle biopsy more than outweighs the small risk involved in the process.

Quantitative estimation of the fibrous tissue in pathologic liver

Since it has been firmly established that in development of alcoholic and some other types of cirrhosis (those based on dietetic deficiency) there is an initial reversible change characterized by fatty vacuolization of liver cells, which is later followed by an irreversible change, characterized chiefly by increasing fibrosis, the expected improvement on dietetic treatment including lipotropic factors, will then depend upon the extent of fibrosis present at the time the therapy is instituted. Having had the opportunity to examine a good number of patients with hepatic cirrhosis, the writer has arrived at the conclusion that neither liver function tests nor histology studies gauge

accurately the extent of damage or fibrosis of the liver. With this in view an attempt has been made to establish a quantitative basis for the estimation of fibrous tissue as an index to the degree of permanent damage of liver (Warren and Wahi, 1947). It has been definitely brought out by chemico-histological correlation that in the lower range of fibrous tissue content there is a fairly good correlation between the amount determined quantitatively and that seen histologically. Above 5 to 6 per cent content of fibrous tissue, it was difficult to judge from histological examination alone, the degree of fibrosis the liver has undergone although this knowledge is of obvious prognostic importance to the patient. Also, in the early stages, it is sometimes difficult to diagnose on the basis of histological examination alone, the presence or absence of cirrhotic process. Chemical determination of fibrous tissue in every puncture biopsy specimen will thus be useful as non-cirrhotic livers have fibrous tissue content of under 3 per cent.

This determination has also been found useful in connection with experimental studies of cirrhosis of the liver (Wahi, 1949). The method is applicable to samples weighing as little as 0.4 gm., and is thus applicable to specimens obtained by puncture biopsy. The technic has already been detailed (Warren and Wahi, 1947).

Summary

The applicability and limitations of certain liver function tests have been discussed.

In the writer's experience needle puncture biopsy has proved as the most useful single method for diagnosis of liver diseases and for supplying the other necessary information to the clinician, *i.e.* differentiation of medical and surgical jaundice when clinical and laboratory data are inconclusive, exact nature and the phase of the lesion in diffuse hepatitis indications for therapy, and complete evaluation of therapeutic regimen in cases of nutritional deficiency disorders.

Quantitative determination of fibrous tissue in cases of hepatic cirrhosis has been found as a useful method of gauging the reversibility of the process and the prognosis of the cases if put on adequate diets. The method can be employed to specimens obtained by puncture biopsy and is thus considered as a laboratory aid of practical importance.

The writer wishes to acknowledge gratefully thanks to Miss Gretchen R. Riese for her constant help in preparation of this paper.

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Medical News

CAUSE OF CANCER

(From Release No. B.F. 944 issued by the British Information Services, Office of the U.K. High Commissioner in India)

Dr. W. E. GYE, Director of the Imperial Cancer Research Fund, in his report for 1948-49 on the work of the Fund's laboratories, states: 'If, as is almost certain, low temperatures kill the delicate mammalian cell but do not affect the virus, then we have no further need for proof that viruses are the continuing cause of cancer'. The report was presented at the annual general meeting of the Governors of the Fund, held at the Royal College of Surgeons in London.

Dr. Gye, who is retiring in the summer after 36 years in cancer research, told the meeting: 'It seems to me that those who have the chance of working on cancer in the future will know what they are working at. As an optimistic elderly man, I suppose I might say that it will become quite possible to treat cancer successfully without the knife'.

The sum of £72,762 (Rs. 9,70,160) was contributed through legacies to the Fund during the year ended 31st January, 1949, and £7,014 (Rs. 93,520) by subscriptions and donations.

T.B. HOSPITAL AT BHAVNAGAR

NAWANAGAR DONATION

BHAVNAGAR, 14th April: The Jamsaheb of Nawanager, Rajpramukh of Saurashtra, declared open the 'Sheth Khushaldas J. Mehta T.B. Hospital', the first of its kind in Gujarat and Saurashtra, at Jinthari (Songadh) near Bhavnagar on Wednesday.

The hospital comprises three general wards of 16 beds each and four first class and 12 second class paying wards. It is equipped with the latest clinical and surgical appliances, an operation theatre and an x-ray plant.

The Jam Saheb announced a donation of Rs. 50,000 on behalf of the Maharani of Nawanager for the construction of four first class wards and also a donation of Rs. 50,000 on behalf of Nagarseth of Jamanagar Popat Dharsi.

He stated that the Saurashtra Government would bear two-thirds of the deficit in the working of the hospital for the first year and 50 per cent of the aggregate deficit thereafter.

Mr. U. N. Dhebar, the Saurashtra Premier, paid tribute to the Maharaja of Bhavnagar for having conceived the idea of starting the hospital.

TUBERCULOSIS IN INDIA

(Reproduced from *Chronicle of the World Health Organization*, Vol. 3, No. 2, February 1949)

THE report of the Bhor Committee revealed that about 500,000 people die annually from tuberculosis in India. This means that the annual number of cases

is approximately two and a half to three million out of a population of 320 million.

The main reasons for this high morbidity rate are threefold: bad housing, lack of sanitation, and malnutrition. Because of a very large population, the housing situation in India is far from satisfactory; two or three families, sometimes comprising as many as ten people, have, in many cases, to share one room. Added to the lack of sanitation, and the food shortage, which is such that many people are living on the verge of starvation, this creates a situation in which the danger of infection is obvious.

There are, further, constant movements of the population between the towns and rural areas: the village people come into the towns for the markets, while the city people make frequent visits to their native villages. This natural tendency has been accentuated by the growth of new industries, which have attracted to the towns large masses of people, most of whom are very poor.

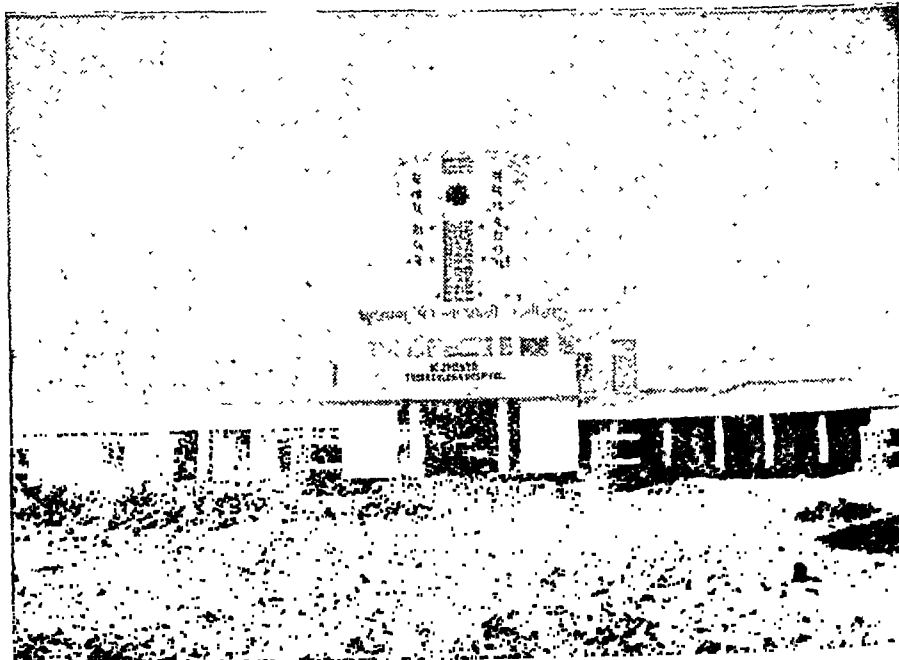
The situation is in general slightly worse in the towns owing to greater overcrowding, but sanitation and nutrition are equally bad in the country, and the danger of infection is increased by the interchange of population between town and country.

It is obvious that no quick solution will be possible for the problems resulting from the constant movement of population and from the industrialization of the country. Both these factors will continue for a long time to confront the health authorities with increasing difficulties. It will take time and colossal sums to improve the sanitation, the housing conditions and the food situation.

It is, however, equally clear that tuberculosis causes untold suffering and serious economic loss in India, and that there is urgent need for action of some kind.

POSSIBLE MEASURES OF CONTROL

The question is: what measures are possible?



Hospital accommodation is quite inadequate. For the treatment of tuberculosis, 500,000 hospital beds would be needed, but at present only 7,000 are available. Attempts are being made all over the country to increase the number of sanatorium beds, but at an optimistic estimate only 30,000 beds could be added within the next few years to the number at present available.

In view of this situation, the authorities have turned their attention to prevention of the disease by BCG vaccination, in the hope of reducing the problem,

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B O M B A Y

within a number of years, to such proportions as to bring its control more within the financial possibilities of the country.

There were, nevertheless, great difficulties in the way of a BCG vaccination campaign in India. The first requirement was tuberculin for large-scale tests; this was not available in India and would have to be imported. Secondly, there was no institute in Asia capable of producing BCG vaccine. Thirdly, there was no trained personnel in India.

TECHNICAL ASSISTANCE BY W.H.O.

To overcome the difficulties, the Government of India requested aid from W.H.O., and in response to this, Dr. W. Gellner and Dr. P. Lind were sent to India to set up a BCG laboratory and to demonstrate BCG vaccination on a mass scale.

The first discussions took place with the Central Government and with Dr. P. V. Benjamin, tuberculosis adviser to the Government of India. Throughout his stay of seven months Dr. Gellner worked in close collaboration with Dr. Benjamin.

During the month of June 1948, the two experts visited a number of cities—Madras, Bombay, Calcutta, Delhi, and Baroda—to contact the provincial health authorities and to discuss plans with them. They met with great interest and co-operation everywhere. Local committees were immediately formed to work out the details, always in consultation with Dr. Gellner and Dr. Benjamin. Financial difficulties seemed to stand in the way of an early implementation of those plans; they were, however, overcome by the readiness of the Central Government to contribute half the cost of the campaigns in the different provinces.

The preparatory work for the establishment of the BCG laboratory actually began several months before the departure of the W.H.O. experts for India. Acting on the assumption that it might be difficult to procure the necessary instruments, materials, etc., in India, they proposed to the government that all the equipment should be purchased in Europe with the object not only of saving time in setting up the laboratory, but also of employing only such equipment as had proved its usefulness in BCG laboratories in Europe, especially in the State Serum Institute, Copenhagen. When the Government of India had agreed to the proposal, all the many articles of equipment—from incubators and analytical scales to filter-paper, ampoules, boxes and labels—were purchased and shipped to India. This operation was so well timed that the shipments landed in India very shortly after Dr. Gellner's and Dr. Lind's arrival there, which made it possible to set up the laboratory in the King Institute at Guindy, Madras, in the record time of a few weeks. Production of the vaccine actually started about the middle of July and the first Indian BCG vaccine was available on 17th August, 1948.

Sir Sahib Singh Sokhey, director of the Haffkine Institute, Bombay, and a member of the W.H.O. Expert Committee on Biological Standardization, visited the new BCG laboratory at the request of W.H.O., and after examining the installations and methods of culture, certified that the BCG vaccine produced at the laboratory conformed to a satisfactory standard.

The all-India BCG vaccination campaign was officially inaugurated in Madanapalle, South India, on 11th August, 1948, by the Indian Minister of Health, Rajkumari Amrit Kaur.* Madanapalle, a town of about 16,000 inhabitants, thus became the scene of the first application of BCG in India within the framework of a general scheme for tuberculosis control, which includes prevention (BCG vaccination), diagnosis by mass radiography, and treatment of discovered cases. From 1st August to 20th October, 1948, approximately 6,000 persons—mostly schoolchildren—were tuberculin-tested and the negative reactors (about 2,000) received

BCG vaccination. Twelve doctors from different parts of the country had been trained in the theory and practice of BCG vaccination.

The work in Madanapalle which aims at the vaccination and mass radiography of the total population, was taken over by an Indian doctor when Dr. Gellner left, towards the end of October 1948, for Delhi to start a second demonstration centre there.

In Delhi, between the end of October and 18th December, 1948, over 10,000 persons were tuberculin-tested and over 5,000 received BCG vaccination; while three doctors were trained in the work. The school-children, who formed the greater part of the tested and vaccinated persons, were dealt with in their schools, while two clinics—one in Delhi and the other in New Delhi—were established for the pre-school children and young adults.

The co-operation which the W.H.O. team gained both in official quarters and among the general population was very good and augurs well for the success of the more extended campaign which is to begin now with the aid of the United Nations International Children's Emergency Fund (UNICEF). This organization—in agreement with W.H.O.—is sending six BCG teams, together with the necessary transport and equipment, to India, where they will be distributed among those capital cities which have already made some preparations for this work.

The function of the UNICEF teams will be to train Indian doctors in the requisite techniques. So long as the Indian health authorities can provide a sufficient number of doctors to work with the foreign teams and to carry on and enlarge their work after the latter have left, it is to be hoped that a systematic BCG campaign will, in the course of time, materially affect the incidence of tuberculosis in India.

CLINICAL TRIALS OF NEW REMEDIES UNDER THE INDIAN RESEARCH FUND ASSOCIATION, NEW DELHI

(Reproduced from *Ind. Jour. Med. Res.*, 36, 2, April 1948, p. 154)

The Indian Research Fund Association have recently appointed a Therapeutic Trials Committee to examine applications received by the Association for the conduct of clinical trials of new remedies and to arrange for trials of suitable remedies. This Committee will encourage and aid impartial clinical trials of biologicals, chemotherapeutic and pharmaceutical agents of Indian or foreign origin, which offer promise in the prevention, treatment and diagnosis of disease. The Medical Research Council of the United Kingdom and the Council of Pharmacy and Chemistry of the American Medical Association have set up similar bodies in their respective countries, and it is considered that the time is now ripe for the initiation of such an organization in India also.

The Committee constituted is as follows:—

1. Dr. M. G. Kini, late Superintendent, Stanley Hospital, Madras.
2. Dr. B. Mukerji, Director, Central Drugs Laboratory, Calcutta.
3. Lieut.-Colonel Jaswant Singh, Director, Malaria Institute of India, Delhi.
4. Dr. J. C. Patel, Hon. Assistant Physician, K. E. M. Hospital, Bombay (*Secretary*).

Before undertaking trials of this nature the Committee will have to (a) decide in the first instance on the suitability of any particular drug for clinical trials and (b) collect data regarding suitability of the place and personnel who should be invited to undertake clinical trials of a particular type of drug.

* *Chron. World Hlth. Org.*, 1948, 2, 229.

The conditions under which the Indian Research Fund Association will be prepared to undertake clinical evaluation of new remedies of Indian or foreign origin submitted by the manufacturers have been drawn up on the analogy of those adopted by the Medical Research Council of the United Kingdom and printed copies of these can be had from the Secretary, Indian Research Fund Association, New Delhi.

To carry out satisfactorily clinical trials of such agents the Association will naturally require the co-operation and help of all medical institutions in India which have facilities for such work and with this end in view these institutions are hereby requested to kindly let the Secretary, Indian Research Fund Association, know at their earliest convenience whether their institutions would be prepared to undertake clinical trials on behalf of this Association when asked to do so. Information regarding facilities available in the medical institutions in India for the conduct of clinical trials which has been invited in the questionnaire already circulated may, therefore, be furnished as soon as possible, direct to the Secretary of the Association. Detailed copies of the questionnaire can be had from the same office.

This subject is of great interest to medical men, biochemists and pharmaceutical chemists in India and their co-operation in the conduct of clinical trials will be highly appreciated.

BLACK-MARKETING IN DRUGS MUST BE STOPPED, SAYS THE HEALTH MINISTER

PHARMACY COUNCIL OF INDIA INAUGURATED

'BLACK-MARKETING in drugs and the use of patent drugs in general by laymen who do not understand their reactions on the body are matters of grave concern to me and my Ministry', said Rajkumari Amrit Kaur, India's Health Minister, inaugurating the first meeting of the Pharmacy Council of India in Delhi on 16th May, 1949.

Dr. K. C. K. E. Raja, Director-General of Health Services, Government of India, who presided over the meeting said: 'The main functions of this Council and of similar organizations such as the Central Medical, Dental and Nursing Councils are to prescribe and enforce desirable standards of training in their respective fields and to ensure that the practice of the profession in each case attained a high standard of professional and ethical conduct'. In all these bodies, he added, the majority of members belonged to the profession concerned, the underlying idea being that the regulation of the profession should mainly be the responsibility of men of standing in their profession.

Thirty members of the Council, who are nominees of the Central and Provincial Governments and those elected by the Inter-University Board and the Medical Council of India, attended the meeting.

Mr. M. L. Schroff, Principal, Birla Colleges of Arts, Science and Commerce, Pilani, was elected Vice-President of the Council and Mr. P. M. Nabar, Dr. H. R. Nanji, Dr. B. Mukerji, Mr. B. V. Patel, and Mr. C. P. Srivastava were elected members of the Executive Committee.

A sub-committee consisting of the following members was appointed to draw up a suitable curricula for training in pharmacy in the country: Prof. B. P. Patel, Prof. S. P. Srivastava, Dr. B. Mukerji, Mr. K. C. Chatterjee, Prof. T. R. Sheshadri, Mr. S. N. Bal and Mr. A. N. Lazarus.

The Council approved the following foreign qualifications in Pharmacy for purposes of registration under the Pharmacy Act:

1. Degrees in Pharmacy obtained from any of the accredited colleges of pharmacy in the U.S.A.

as issued by the American Council of Pharmaceutical Education from time to time;

2. Degree of B.Pharm. or B.Sc. (Pharm.) of a British University; and
3. Diplomas of Chemist and Druggist and Pharmaceutical Chemist of the Pharmaceutical Society of Great Britain.

The Council further authorized the Executive Committee to approve such other foreign qualifications in Pharmacy as it may consider satisfactory for purposes of registration.

RADIO-ACTIVE ISOTOPES FOR WORLD BUYERS

(Abstracted from Release No. 1034 issued by the British Information Services)

Britain can now supply radio-active isotopes from the new atomic pile at Harwell to overseas markets. Already 12 British industrial groups are using isotopes for experimental and measurement purposes. They are also being used extensively for medical purposes and experimentally in agriculture and marine biology.

NEW DEVICE TO MEASURE BLOOD CELLS

(From Release No. B.F. 1018 issued by the British Information Services)

AN entirely new scientific instrument called a halometer which has been designed for the rapid and accurate measurement of the red cells in human blood has been perfected by a London manufacturer.

The measurement of the diameter of blood cells by halometry depends on laws of diffraction. When a small source of light is viewed through a thin blood film on a glass slide, a circular coloured pattern, or halo, is seen. The angular diameter of this halo is inversely proportional to the diameter of the blood cells and it is this which the halometer measures.

BIG FALL IN DIPHTHERIA DEATH RATE

(Abstracted from Release No. B.F. 1026 issued by the British Information Services)

FOR the seventh consecutive year deaths from diphtheria in Britain have been the lowest ever recorded. Last year they totalled 150 compared with 2,641 in 1941.

It was in that year that the British Government initiated a national campaign for immunizing infants against this deadly disease. Since then outbreaks of diphtheria have also shown an equally spectacular and steady reduction. In 1941, nearly 51,000 cases were registered. Last year there were only 8,034.

SIXTH INTERNATIONAL CONGRESS OF RADIOLOGY

THE Sixth International Congress of Radiology will be held in London from 23rd to 29th July, 1950. The headquarters of the Congress will be at the Central Hall, Westminster, which will also house an extensive Scientific Exhibition. The Technical Exhibition of apparatus will be located in the Halls of the Royal Horticultural Society nearby.

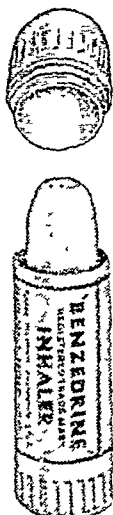
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Information has been received by the Director-General of Health Services that the health authorities in Siam have declared Calcutta infected with cholera.

In order to avoid delay and inconvenience on entry into Siam, passengers leaving Calcutta for Siam are advised to be in possession of cholera inoculation certificates showing that inoculation has been performed not less than seven days and not more than six months prior to arrival in Siam.

The health authorities in Turkey have agreed to withdraw the anti-plague certificate requirement in respect of passengers from India. Anti-plague measures such as medical inspection and surveillance prescribed under the International Sanitary Convention will, however, continue to be applied to such travellers at the discretion of the Turkish health authorities.

200TH ANNIVERSARY OF VACCINATION PIONEER

(From Release No. B.F. 1138 issued by the British Information Services)

*To commemorate the 200th anniversary of the birth of Dr. Edward Jenner, the British physician, who introduced to the world the technique of vaccination, an exhibition has been arranged in London.

It was in 1798 that Dr. Jenner first placed before the world the results of his researches into the possibilities of vaccination. This new technique soon spread to all parts of the civilized world and by 1800 had become recognized medical practice.

It was not till about 80 years later that Pasteur extended Jenner's discovery by using vaccination against cholera and anthrax. It was he who proposed, at a meeting of the Medical Congress in London, that vaccination be officially adopted as the term for this method of conferring immunity from infectious diseases. He suggested this as a 'homage to the merit and immense services rendered to medicine by one of England's greatest men, Dr. Jenner'.

TEACHING SURGERY THROUGH TELEVISION

(From Release No. B.F. 1160 issued by the British Information Services)

MEDICAL history has been made at Guy's Hospital, London, where the most important development yet known in the teaching of surgery has been demonstrated. It involved the installation of a permanent television camera in the operation theatre, the equipment used being the only appliance of its kind in the world.

Details of an actual operation for appendicitis were clearly seen by viewers in another part of the hospital. It was conducted by the Director of the Surgical Department who gave an explanation of what was going on. He showed how to hold a surgical knife, and how to stem bleeding.

This method of instruction will enable students to see operations in much greater detail than before and from an angle hitherto impossible. They can watch actions from a position immediately above the surgeon's hands while listening to verbal explanation.



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CARDIOLOGICAL SOCIETY OF INDIA RESEARCH FELLOWSHIP of the value of Rs. 3,000 (Rupees Three Thousand only) for the year 1949-50 has been awarded to Dr. Miss H. M. Colabawalla of the K. E. M. Hospital, Bombay.

THE FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

THE following students were declared to have passed the D.T.M. Examination, Session 1948-49 :—

Passed with distinction

Pabitra Kumar Raychaudhuri, M.B. (Cal.), Private Practitioner, Awarded the 'Chuni Lal Bose' Gold Medal, 1949.

Passed

(Arranged in alphabetical order)

Bejoy Kumar Banerjee, M.B. (Cal.), Private Practitioner.

Chittaranjan Banerjee, M.B. (Cal.), Private Practitioner.

Prasanta Kumar Banerjee, M.B. (Cal.), Private Practitioner.

Radhika Nath Basu, M.B. (Cal.), Private Practitioner.

Abinash Chandra Bhadra, L.M.F. (Dacca), L.T.M. (Cal.), Private Practitioner.

Rajindar Kumar Chatrath, M.B., B.S. (Punjab), Private Practitioner.

Nariman Erachshah Cooper, M.B., B.S. (Bom.), Assistant Surgeon, B. B. & C. I. Railway.

Kripa Nath Das, L.M.P. (Dibrugarh), Assistant Medical Officer, Sagurnal Tea Estate, Sylhet.

Agnelo F. D'Souza, M.B. (Cal.), Private Practitioner.

Satish Chandra Shankerrao Dighe, M.B., B.S. (Bom.), Private Practitioner.

Kali Bhushan Dutta, L.M.F. (Dacca), M.B. (Cal.), Private Practitioner.

Satya Ranjan Dutta, M.B. (Cal.), Assistant Medical Officer, Raniganj Coal Association Ltd.

Mritunjay Prosad Ghose, M.B., B.S. (Lucknow), Private Practitioner.

Rabindra Nath Ghosh, M.B. (Cal.), Private Practitioner.

Chittaranjan Gupta, M.B. (Cal.), Private Practitioner.

Narayan Das Gupta, M.B. (Cal.), Private Practitioner.

Madhu Sudan Gupta, M.B., B.S. (Patna), Private Practitioner.

Bhola Nath Haldar, L.M.F. (Bengal), M.B. (Cal.), Private Practitioner.

Bhagwan Ganesh Kane, L.M.P. (C.P.), Assistant Medical Officer (Pathologist), Mayo Hospital, Nagpur.

Sharnagat Singh Khandpur, L.M. & S. (Punjab), Private Practitioner.

Hari Das Koley, M.B. (Cal.), D.P.H., Private Practitioner.

Biswanath Mandal, L.M.F. (Bengal), Private Practitioner.

Satyendranath Mitra, M.B. (Cal.), Demonstrator of Pathology, Lake Medical College, Calcutta.

Amiya Kumar Mukhopadhyaya, M.B. (Cal.), Private Practitioner.

Rabindra Nath Mukhopadhyaya, M.B. (Cal.), Private Practitioner.

Santosh Kumar Mukhopadhyay, M.B. (Cal.), Private Practitioner.

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Birendra Nath Pattanayak, M.B. (Cal.), House Physician, Marwari Hospital, Calcutta.

Amarendra Nath Ray, L.M.F. (Bengal), Private Practitioner.

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Gurdev Singh, M.B., B.S. (Punjab), Assistant Surgeon, In-charge, Civil Hospital, Rajpura.

Har Narain Singh, B.Sc., M.B., B.S. (Punjab), Private Practitioner.

Sarah Thomas, L.M.P. (Vellore), Private Practitioner.

Rabindra Kumar Tarat, L.M.P. (Dibrugarh), Private Practitioner.

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ALL-INDIA CONFERENCE OF INDUSTRIAL MEDICINE

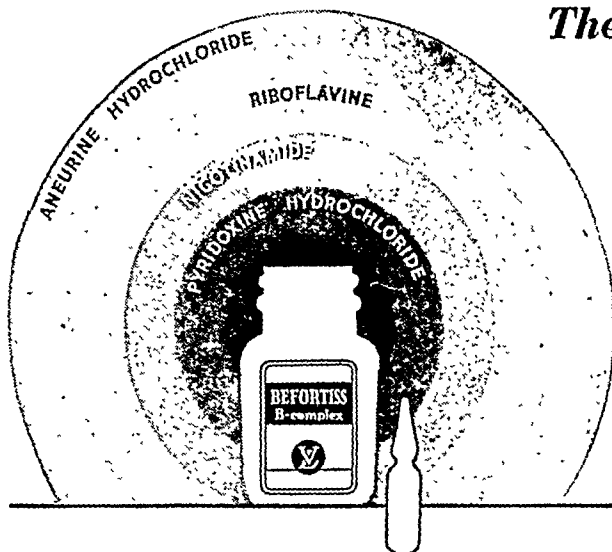
At its March meeting, the Council for the Society for the Study of Industrial Medicine decided to endeavour to hold an All-India Conference of Industrial Medicine in the winter of 1949 at Jamshedpur. The object is to bring together all the medical officers associated with industry, and to exchange ideas and work in co-ordination, thus making their work more effective and more widespread. At present when our country is being industrialized the need for co-ordinated scientific planning of industrial medicine is vital. At this conference, as the name indicates, are invited all the medical officers associated with industry throughout the country. It is, therefore, the duty of all the progressive industrial concerns to send delegates to this conference and every doctor associated with industry should try to participate.

The success of this long over-due conference depends on all the industrial concerns and the medical officers in industry, whose support is solicited.

Jamshedpur, the biggest and one of the oldest industrial cities in India, is an ideal choice for the first All-India Conference of Industrial Medicine. The Council of the Society for the Study of Industrial Medicine will make arrangements for accommodation, etc. All those interested in the progress of industrial medicine are invited to participate. Those who wish to attend the conference and those who wish to read papers on any of the different aspects of industrial

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medicine are requested to communicate to the Honorary Secretary, Society for the Study of Industrial Medicine, c/o Tata Main Hospital, Jamshedpur, as soon as possible so that final arrangements may be made and V.I.P.s approached. The provisional dates fixed for the conference are 22nd and 23rd December, 1949.

The Indian Medical Gazette Fifty Years Ago

CALCUTTA HOSPITALS

(Reprinted from the *Indian Medical Gazette*,
Vol. 34, 1899, No. 7, July, p. 261)

COLONEL HENDLEY's report on the Calcutta Medical Institutions for 1898 shows that 123,567 men, 39,706 women and 47,977 children were treated as out-door and in-door patients during the year, as compared with 177,710 men, 48,981 women and 63,010 children treated in 1897, showing a total decrease of 78,511, which is attributed to the plague-scare having temporarily reduced the population for some months. The number of Europeans and Eurasians treated increased by 134 and 1,482 respectively, while that of Mohammedans and Hindus diminished by 25,933 and 52,303. It appears from Colonel Hendley's report that the attendance of female patients increases, as might be expected in India, in proportion to the privacy secured in the consulting rooms. The total number of beds available for in-door patients is 1,721, while the average number of beds occupied was 1,158. In Calcutta, 259 per thousand of the population were treated as out-patients. The medical relief given in Calcutta compares favourably with that given in the large towns in England, though it is probable that, with better arrangements, more women would attend the hospitals. The death-rate for all the hospitals, excluding the Eye Infirmary, was 13.2 per cent of the number of patients treated against 16.4 in the former year. Marked variations, depending on the class of patients admitted, occurred at the several institutions. Thus the death-rate for men was 0.86 at the Police Hospital, 21 at the Campbell Hospital and 22 at the Howrah General Hospital. Similarly, in the case of adult women, the Dufferin Victoria Hospital shows a rate of 0.76 and the Campbell Hospital of 30. There has been a considerable decrease in the death-rate of the Howrah General Hospital, due it is reported to the comparative healthiness of the district in 1898, and to the admission of fewer moribund persons. Smallpox was less prevalent during the year, and the number of patients admitted into hospitals suffering from the disease fell from 218 to 37. With the exception of one case at the Mayo Native Hospital, the rest were

treated at the Campbell Hospital. There was only one European admitted to the Campbell Hospital, against 41 in the previous year. Among those attacked, 23 were unprotected, and 11 of them, or 47.82 per cent, died. Of 10 persons who had been vaccinated, one died, but the marks of vaccination were very faint. The total death-rate was 32 against 30 in the previous year. The number of admissions for cholera decreased from 1,200 to 227, and the death-rate from 55 per cent to 54 per cent. The decrease in admissions is most marked in the Campbell Hospital, where only 89 cases were treated against 535 in the previous year. Among the patients there were 17 Europeans and Eurasians, of whom 10 died, a ratio of 59 per cent. It is satisfactory to note that no case of cholera originated in any of the institutions during the year.

The surgical operations decreased from 25,745 to 21,610, owing to the falling off in the attendance of patients due to the plague-scare. Death followed in 154 cases, giving a percentage of 0.71 against 0.70 in the previous year. The largest number of operations was performed at the Medical College Hospital, where the death-rate was 0.96 against 0.78. The increase is attributed to a larger number of operations of a serious nature having been performed. Colonel Hendley proposes a change on the system of recording the surgical operations. In the Eden Hospital the number of women and children admitted as in-door patients decreased from 1,535 to 1,372. Of these, 200 were Europeans, 519 Eurasians, 582 Hindus and Mohammedans. The death-rate for Europeans and Eurasians is given as 5.14, and that for all others as 10.37 against 4.99 and 10.18 of the previous year. The death-rate for native children fell from 33.64 to 25, although 8 children were admitted in a moribund condition. The number of confinement cases fell from 616 to 582, of which 18 were fatal as compared with 22 in the previous year. There were nine fatal cases of septicæmiæ, of which two originated within the hospitals. There were 1,104 operations performed, against 1,146 in the previous year. It is satisfactory to note that, of the 14 cases in which ovariectomy was performed, 11 proved successful.

The Lieutenant-Governor, in reviewing the report, is glad to notice that numerous improvements have been carried out at the several hospitals. Very large sums are being spent on the reconstruction and improvement of the Presidency General and Medical College Hospitals, which he does not doubt will greatly add to their efficiency and usefulness, but he is pleased to see that smaller matters do not escape the notice of Colonel Hendley, and that almost everywhere little changes are being introduced, which do not cost much, and yet which all help to promote the comfort of the patients.

[Some of the topics under this heading are not exactly current. They have been held up because of special numbers for which they were not suitable. They are included because of their importance.—
EDITOR, I.M.G.]

Current Topics, Etc.

Dangerous Talc

(Abstracted from the *British Medical Journal*, i, 5th June, 1948, p. 1090)

It is only within the last forty years that the use of sterilized rubber gloves has become a standard part of surgical operative technique. In thus reducing the risk of bacterial infection the surgeon has unwittingly introduced a new wound hazard whose harmful potentialities are only now becoming recognized. It is customary to sterilize gloves by steam, and talc powder is used to prevent them from adhering and to facilitate the insertion of the hand. The outside of the gloves is left covered with adherent talc and the tip of each finger commonly contains a somewhat larger quantity. Since talc sticking to the gloves after steam sterilization is not easily removed by rinsing in saline or water, handling the exposed tissues with such gloves introduces talc into the wound. If in the course of operation the fingertip of a glove is perforated, the talc accumulated inside may escape into the wound in dangerous amount, particularly if the puncture is unnoticed.

The effects of talc in the tissues were first recognized by Antopol in 1933 and confirmed by Feinberg and Gardner four years later. German described the characteristic follicular giant-cell reaction and by 1943 had collected 50 cases of talc granuloma following laparotomy. He showed that the talc particles often became widely distributed in the abdominal cavity before setting up a reaction. A new aspect of the unforeseen harm done by talc was revealed by Roberts, who showed that granulomatous lesions of the Fallopian tubes might result from the intratubal migration of talc particles introduced during a previous appendicectomy, and that sterility was the usual consequence. At a recent meeting of the Association of Clinical Pathologists, Cappell and Faulds both mentioned the occurrence of tubal silicious granuloma following diagnostic insufflation of the Fallopian tubes.

Three papers on the subject of silicious granuloma appear in this issue of the journal. Mr. Arthur Mackey and Dr. J. B. Gibson draw attention to the greater density and severity of adhesions after laparotomy as compared with those resulting from purely bacterial inflammation in the unopened abdomen and they provide striking evidence that such adhesions may be brought about by talc within so short a period as 13 days. Dr. W. Walker describes fatal intestinal obstruction occurring only seven weeks after laparotomy and shows that the adhesions causing the fatality contained abundant talc crystals. Dr. G. Harvey Smith adds to the tubal group a case previously reported as tuberculosis (associated with carcinoma of the uterus).

These papers emphasize that talc can produce a variety of lesions, some of which may fortuitously become lethal. The finding of an acceptable substitute is therefore an urgent problem. Lycopodium powder is equally harmful and potassium bitartrate, proposed by Seelig as a substitute, is unacceptable because of its macerating effect on the hands. What is wanted is a colourless powder with the lubricant properties of talc or graphite, unaffected by steam sterilization, and giving rise to no reaction in the tissues. The problem is one first for the chemist, but, until an acceptable substitute is found, surgeons aware of the potential

dangers of talc could minimize the risk by insisting that there should be no excess powder in the tips of their gloves before inserting the hands, and by removing all surplus talc from gloves before handling the exposed tissues.

A New Substance for Asthma

(Abstracted from the *British Medical Journal*, i, 7th February, 1948, p. 261)

A FURTHER addition to anti-asthmatic substances is a derivative of adrenaline. Adrenaline has an amine group at the end of its side chain in which one of the hydrogen atoms is substituted by $-\text{CH}_3$. Konzett found that replacement of this methyl group by an isopropyl group resulted in a substance which was 10 times as powerful as adrenaline in relaxing bronchial spasm produced in the anaesthetized dog. He examined other related substances: N-ethyl adrenaline was 3 times as potent as adrenaline; N-propyl- and N-butyl adrenaline were about equal in potency to adrenaline; and, finally, N-isobutyl adrenaline was about 10 times weaker. The substance neosynephrine or metasympatol, which differs from adrenaline in having only one $-\text{OH}$ group in the benzene ring, was also found to develop great power to relax the constricted bronchioles when an isopropyl group replaced the methyl group in the side chain.

Isopropyl adrenaline (now manufactured in the U.S.A. as 'isuprel') has an action on the heart similar to that of adrenaline, but, unlike adrenaline, it causes a fall of blood pressure. This effect is not likely to be appreciable when isopropyl adrenaline is used therapeutically, since the amount required is so small. The properties described by Konzett have been confirmed.

Risks of Dicoumarol Therapy

(From the *British Medical Journal*, i, 22nd May, 1948, p. 988)

THROMBOSIS of the leg veins, with the pulmonary emboli which may follow, was shown by Belt to be as frequent a cause of morbidity and death in medical wards as in surgical. The introduction by Crafoord of heparin as a prophylactic against thrombosis led to a considerable reduction of thrombo-embolic complications in surgery. The cost of heparin, however, still remains almost prohibitive, and supplies are certainly nothing like adequate to allow its general use in the prophylaxis and treatment of leg vein thrombosis. For this reason other anticoagulants are being sought, and dicoumarol, which has the advantage that it can be given by mouth, is now being widely used. Dicoumarol prolongs the prothrombin time, and, though it takes about two days for this effect to develop, the first 48 hours can be conveniently covered by heparin.

One of the most important indications for treatment with anticoagulants is coronary thrombosis. If the blood can be prevented from clotting, the thrombosis may remain limited, intracardiac thrombi may not form, and pulmonary emboli, which frequently occur during the period when these patients are confined to bed, may be avoided. Glueck and his colleagues recently reported that in 44 control patients with coronary thrombosis, thrombo-embolic complications occurred in 12, while in 44 treated with anticoagulants, only 3 developed these complications. The mortality of the control group was 45 per cent, while in those treated with anticoagulants, it was 20 per cent. Though these figures may not satisfy statistical demands, it is only by the accumulation of the results of careful clinical studies that final decisions will be reached on this important problem.

The mechanism by which dicoumarol interferes with the clotting process depends on its action in preventing



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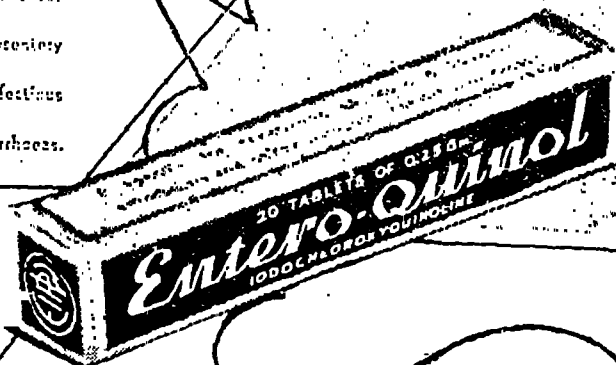
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prothrombin formation by the liver. The drug can only be given safely in hospital, as the margin between an effective therapeutic dose and a toxic dose is very narrow indeed. Furthermore, there is no easy way of standardizing dosage in any individual patient, and daily estimations of prothrombin time are necessary. There can be no relaxation of this precaution. Patients taking 200 mg. daily may retain a satisfactory prolonged prothrombin time for ten days or a fortnight, and suddenly, without alteration of dosage, it is found that the prothrombin time has reached the danger level. Alternatively, in spite of keeping to the same dose, the prothrombin time may suddenly fall for no apparent reason, with the possible appearance of further thrombosis.

A recent report from Zurich by Koller and Pedrazzini emphasizes the danger of uncontrolled dicoumarol treatment. A patient who had received 0.3 g. of dicoumarol daily for 14 days developed epistaxis, gross hæmaturia, and blood in the stools. Subcutaneous and subconjunctival hæmorrhages, together with other purpuric manifestations such as positive capillary resistance test and failure of clot retraction, were also present. In spite of the administration of a vitamin K preparation no change took place in prothrombin time, and it was only after a week, during which several blood transfusions were given, that the patient ultimately recovered. Liver function tests were mostly negative during this period. This report is a useful reminder of the necessity for the strictest control of anticoagulant therapy. Fatalities are otherwise likely to occur, and the Zurich patient was fortunate to recover. Though dicoumarol seems to have earned its place in therapy at the moment, it is sincerely to be hoped that a safer anticoagulant will be found before long.

Physical Treatment of Arthritis

By W. M. SOLOMON

(Abstracted from the *Journal of the American Medical Association*, Vol. 137, 8th May, 1948, p. 128)

HEAT in any form increases the circulation to the part, relaxes the tissues and relieves pain. That certainly justifies its use. Most forms of heat are applied at least once a day, and two or three times a day are even better. Many methods of applying heat are available. The infra-red lamps are perhaps the ones most frequently employed. It is well to remember that the bulb type or the incandescent filament lamp penetrates to a greater depth than the so-called non-luminous form which is made up of a solid iron rod or plate.

A treatment should be at least thirty minutes to secure the best physiological benefit. The practice of using a hand lamp for five to ten minutes is a waste of time.

A more elaborate and expensive means of applying infra-red radiation is by the baker, which is merely an oven-like affair, in which four to eight incandescent bulbs are suspended. This is most useful if both knees or the lower extremities are to be treated. It is also useful for the back.

Another simple and inexpensive means of applying heat to joints is by the use of paraffin. All that is required is eight to ten pounds (3.6 to 4.5 kg.) of paraffin such as is used to seal jelly or fruit jars and a container to heat it. A double boiler is more convenient and safer, since this prevents setting the paraffin on fire. The wax is melted and then removed from the fire, and when a thin film forms on the surface, it is at the right temperature for the patient to use. If it is for the hands, he dips them in the paraffin and then removes them when the paraffin solidifies. This is repeated eight to ten times until a glove of about one-fourth inch (0.64 cm.) or so has formed. The hands can then be wrapped in a bath towel for fifteen

or twenty minutes, after which the paraffin is peeled off; it can be used over and over again. For joints other than the hands, a paint brush may be employed and the paraffin painted on.

When numerous joints are involved, as in rheumatoid arthritis, the full tub bath can be recommended, since it heats all the joints and has the additional advantage that while the patient is in the tub, he can be urged to exercise the affected joints. The temperature of the water should not exceed 100°F., and the treatment should last about twenty minutes.

MASSAGE

After the use of heat in any of these forms, massage should follow. Physicians neglect massage because they know so little about this measure and more often than not have never been told or shown how to give a massage.

Massage is capable of producing definite physiologic effects which are most beneficial to the arthritic patient. The ideal would be to have a physical therapist give the massage daily, but this would be an expense which but few arthritic patients could tolerate; therefore some member of the family should be instructed in the method of giving a massage. In most instances the amateur masseuse can do a reasonably good job. If the physician cannot give instructions for massage he owes it to his patient to see that a physical therapist shows the methods to someone in the family.

EXERCISE

After the heat has been applied and the massage has been given, the patient is ready for the exercises. This is one of the most valuable forms of physical therapy, particularly for the patient with the rheumatoid arthritis. Nothing is more pathetic than the plight of a patient with rheumatoid arthritis who has deformities and contractures which in many instances might have been prevented. It is believed that if such a patient will go through the full range of motion once each day for all the joints involved, he can be reasonably assured that he will not be a cripple. In the early stages of the disease the exercises are relatively simple and cause little pain, but if the patient is not properly instructed, he will delay movement of joints in hope that the pain will disappear. In too many cases it is then too late, for fibrosis, adhesions and even bony ankylosis may have occurred. In my opinion irreparable damage is done by advising the patient to go to bed and remain there until all swelling or pain has disappeared. This may take thirty or forty years. Immobilization results in weakness and loss of muscular tone and leads to atrophy and eventually deformities. On the other hand, a patient with rheumatoid arthritis is warned against too much exercise. Often such a patient exercises a joint as much as possible, hoping thereby to prevent stiffness. This also is incorrect.

During the relatively acute stage the exercises are done slowly and increased according to the tolerance of the patient. It is well to remember that certain muscle groups, such as the flexors and adductors, lead to deformities; therefore exercises for their antagonists—namely, the extensors and abductors—should be stressed. In the beginning merely going through one or two movements for each joint will be sufficient; later this can be increased to several times during each day and, finally, by weight-bearing exercises.

Exercise for the joints, although most important, is monotonous. There is no substitute for active movement of each individual joint; however, additional exercises may be suggested in the form of occupational therapy, which makes the patient forget the exercise in an effort to accomplish a task. This not only supplies the physical activity but has a psychological incentive as well. By the proper methods this form of therapy can be directed to insure exercises for any joints desired. Occupational therapy is not confined to the hospital but should be used in the home, since many simple devices are available that can be suited to the interests of each patient.

Chloroquine Diphosphate

(From the *Journal of the American Medical Association*, Vol. 136, 17th April, 1948, p. 1049)

CHLOROQUINE DIPHOSPHATE.—Aralen diphosphate-winthrop.-7-chloro-4-(4-diethylamino - 1 - methylbutyl-amino) quinoline diphosphate.— $C_{21}H_{28}ClN_3O_3P_2$.—M. W. 515.88.

Actions and uses.—Chloroquine diphosphate is highly active against the erythrocytic forms of *Plasmodium vivax* and *Plasmodium falciparum*. It does not prevent relapses in vivax malaria, nor will it prevent the establishment of vivax infection when administered as a prophylactic. It is, however, effective in vivax malaria as a suppressive agent and, for the termination of acute attacks, significantly lengthening the interval between treatment and relapse.

In falciparum malaria, chloroquine diphosphate abolishes the acute attacks and effects complete cure of the infection.

Chloroquine diphosphate has approximately three times the activity of quinacrine hydrochloride against standardized strains of *P. vivax* and *P. falciparum*.

Chloroquine diphosphate is rapidly and completely absorbed by the gastro-intestinal tract. Some of it is excreted slowly in the urine. Considerable amounts are deposited in the organs and tissues, and it is concentrated in nucleated cells, particularly those of the liver, spleen, kidneys and lungs.

Dosage.—Chloroquine diphosphate is usually administered orally either before or after meals. For suppression of vivax malaria a weekly dose of 0.5 gm. given at exactly seven-day intervals is recommended.

Chloroquine diphosphate is metabolized in the body, but this occurs slowly and the drug may be detected in body tissues for more than a week after discontinuing medication. The drug is well tolerated in therapeutic doses and does not produce cinchonism or discolour the skin. However, there may be mild headache, pruritus, visual disturbances and gastro-intestinal complaints following therapeutic doses. Blurring of vision and difficulty in focusing are occasionally observed following prolonged administration. None of the side reactions appears serious, and all have been of a reversible nature.

For the treatment of acute attacks of malaria due to *P. vivax* and *P. falciparum*, an initial dose of 1 gm. followed by an additional 0.5 gm. after six to eight hours and a single dose of 0.5 gm. on each of two consecutive days (total of 2.5 gm. in three days) is sufficient to eradicate most infections with *P. falciparum* and to terminate an acute attack of vivax malaria. In the latter, freedom from clinical attacks may be maintained thereafter by administration of suppressive doses (0.5 gm. weekly).

Tests and standards.—Chloroquine diphosphate occurs as a white, crystalline powder possessing a bitter taste. It melts in the range 193 to 195°C. Two modifications of chloroquine diphosphate are obtainable. The second form melts at 215 to 218°C. It is freely soluble in water and practically insoluble in alcohol, benzene, chloroform and ether. The pH of a 1 per cent solution is about 4.5.

Dissolve about 50 mg. of chloroquine diphosphate in 3 cc. of water. Add a few drops of ammonium molybdate test solution: a white precipitate develops immediately.

Dissolve 20 mg. of chloroquine diphosphate in 20 cc. of water. Add 5 cc. of a saturated aqueous solution of picric acid: a yellow precipitate forms immediately. Filter off the precipitate, wash with water and air-dry on the filter funnel: the product melts from 205 to 210°C. (Caution!).

Dissolve 0.25 gm. of chloroquine diphosphate in 50 cc. of water. Add 1 cc. of strong ammonia solution and

extract with two 30 cc. portions of cyclohexane. Evaporate the cyclohexane solution to dryness on the steam bath. Place the residual oil in a vacuum desiccator over phosphorus pentoxide and allow to stand overnight to permit crystallization: the solid material melts at a temperature of 87 to 90°C.

Dry about 0.25 gm. of chloroquine diphosphate, accurately weighed, in vacuum over phosphorus pentoxide at room temperature for forty-eight hours: the loss in weight does not exceed 2 per cent.

Dissolve about 0.2 gm. of chloroquine diphosphate, accurately weighed, in 50 cc. of water. Dissolve 1.5 gm. of bismuth oxynitrate in 10 cc. of nitric acid and dilute to 100 cc. with water. Add 50 cc. of the bismuth solution to the solution of chloroquine diphosphate. Digest for two hours on the steam bath, filter into a tared Gooch crucible and wash with dilute nitric acid (2 cc. to 100 cc.). Wash successively with water, alcohol and ether. Dry in an oven at 100°C. for two hours: the phosphorus content is not less than 11.8 per cent or more than 12.25 per cent.

Weigh, accurately, about 0.2 gm. of chloroquine diphosphate. Dissolve in 50 cc. of water, transfer to a separatory funnel. Add 5 cc. of ammonium hydroxide and extract with 25, 20, 15, 10 and 10 cc. portions of ether. Drain the combined ether extract through a cotton pledget into a 100 cc. tared beaker. Evaporate the solution on the steam bath to dryness and finally heat at 100°C. for thirty minutes: the residue calculated to chloroquine diphosphate is not less than 98 per cent or more than 102 per cent.

CHLOROQUINE DIPHOSPHATE TABLETS

Grind ten tablets in a mortar. Weigh, accurately, about 0.3 gm. of the pulverized tablets. Dissolve in about 50 cc. of water, filter and wash the residue with about 20 cc. of water. Transfer to a separatory funnel, add 5 cc. of ammonium hydroxide and extract with 25, 20, 15, 10 and 10 cc. portions of ether. Drain the combined ether extracts through a cotton pledget into a 100 cc. tared beaker. Evaporate the solution on the steam bath to dryness and finally heat at 100°C. for thirty minutes: the residue, calculated to chloroquine diphosphate, is not less than 95 per cent or more than 105 per cent.

Risks of Sternal Puncture

(From the *Lancet*, i, 10th April, 1948, p. 566)

At an inquest at Battersea six months ago the coroner described sternal puncture as 'a highly dangerous procedure to obtain pathological material'. The published work does not confirm this view, for only two previous fatalities have been reported. Considering the frequency of the operation, which was introduced in 1927 by Arinkin, the mortality is low, though it is possible that some deaths have not been recorded and have not even reached the coroner's court. Often the operation is performed on gravely ill people, so that death might readily be attributed to the disease under investigation. Nevertheless, it can be assumed that fatalities are extremely rare.

The fatal case reported by Meyer and Halpern was in a man of 51 who had myeloid leukaemia. At the time of the puncture he was extremely apprehensive, for two previous attempts had failed. This time the marrow was found on the second trial, but immediately the needle was removed the patient became faint, dyspnoeic, and cyanotic, and he died within a few minutes. A terminal electrocardiogram showed bizarre ventricular complexes indicating severe conduction defects, with progressive bradycardia until asystole was complete. Permission for necropsy was refused. Death was thought to be due to a fatal cardiac inhibitory reflex induced by fear, and it was recommended that a mild sedative should always be given before the operation. In the second case, described by Scherer

and Howe, man of 31 with a malignant teratoma of the anterior mediastinum, had a similar story of previous unsuccessful attempts, but on this occasion puncture was again unsuccessful. 'Shortly afterwards' the patient became pale and semicomatose with dilated pupils and noisy breathing. He died about half an hour after the puncture. Necropsy revealed that the needle had perforated the sternum and pericardium and had entered the anterior wall of the right ventricle to a depth of 5 mm.; there was a large hæmopericardium. In this case the operator, experienced in the difficulties to be met with in the sternums of patients with osteosclerosis, Paget's disease, and sclerosing metastatic tumours, tried at several levels between the third and fourth rib, the needle being inserted sometimes to a depth of $\frac{3}{4}$ inch. He was unsuccessful because of the extensive fibrous-tissue replacement of the marrow cells, and the mediastinal tumour may possibly have been pressing the heart on to the undersurface of the sternum. Since this accident, Scherer and Howe advise, in cases of difficulty, that the needle should be inserted into the sternum in the usual area from below at an angle of 45° , to reduce the danger of deep penetration.

Experience teaches the operator the feel of a normal sternal puncture, and it varies with the age of the subject. In older patients the needle meets with increased resistance and greater care is needed. Some diseased marrows are fibrotic, or perhaps bony hard, while others, as was found in the fatal case last September, are soft and porous. Individual variations in the depth of the sternum are less common than variations in the depth of the parietes, but, whereas the latter can be readily felt, the former can be discerned only through one's sense of touch projected through the needle. Anomalies of the mediastinum and aberrant vessels are not likely to be encountered. All the same as with every procedure and treatment which carries any risk whatever, sternal puncture should not be done unless the full indications are present. A sternal puncture is justified in any case of refractory or obscure anæmia, atypical leukaemia, and 'storage' disease, and in some protozoal diseases (systemic leishmaniasis and malaria, especially malignant tertian). It is doubtful if it can often be justified for medullo-culture, though Ling and Hsueh suggest that it should be more widely used in systemic bacterial infections, especially when blood-culture is unsuccessful. Scherer and Howe, on the facts before them, were inclined to attribute Meyer and Halpern's fatality, like their own, to cardiac tamponade; and they may be right. Nevertheless, the fact that sudden collapse and death due to reflex cardiac inhibition is a possible sequela of sternal puncture has to be reckoned with. Nor should the risk of infection be overlooked, for it is met with from time to time when medullo-infusions are given. Finally, it should be remembered that some of the diseases which call for diagnostic sternal puncture may be associated with a bleeding tendency, so that relatively trivial sternal trauma, which might be expected to heal without difficulty, may lead to a fatal hæmorrhage.

(For fatal sternal puncture see this journal, 82, 459.)

Blood Transfusion with Unsuspected Rh Sensitivity

By D. L. DAVIES

(Abstracted from the *Medical Journal of Australia*, Vol. 1, 3rd January, 1948, p. 13)

A MALE patient, aged thirty-one years, was admitted to the Repatriation General Hospital, Springbank, South Australia, in June 1947, and gave the following history. In October 1945, he had vomited about one pint of altered blood, and his stools were tarry for two days; his condition was investigated, but no evidence of peptic ulcer was found.

In view of the patient's general condition and lowered hæmoglobin value, a blood transfusion was considered necessary. He had not before received a blood transfusion. The patient's blood group was O (IV), and by direct matching for twenty minutes at room temperature his serum was found to be compatible with the red cells of four donors of group O (IV). Four pints of blood were given over a period of twenty-four hours without any reaction, and his general condition improved.

Twenty-four hours after cessation of the transfusion he was slightly jaundiced. Twenty-four hours later again he was deeply jaundiced, but felt well; the hæmoglobin value was then 60 per cent. His urine was chocolate coloured and turbid, and contained much bilirubin and methæmalbumin. Examination of his blood revealed gross hæmolysis.

Investigations were carried out to discover the explanation of the hæmolysis. In the first place, the patient on being further questioned, said that at a malaria experimental station at Rocky River in January 1944, he had received 20 millilitres of malarial blood by intramuscular injection. Next, blood and serum taken from the patient during the stage of intense jaundice were sent to the Institute of Medical and Veterinary Science, Adelaide, for examination. The patient's blood was there found to belong to group O (IV) and to be Rh-negative. The following findings were obtained on examination of the serum. The anti-A agglutinin titre was 1/16 (++), 1/32 (+), 1/64 (+). The anti-B agglutinin titre was 1/16 (++), 1/32 (+), 1/64 (+). Anti-Rh agglutinins were present to a titre of 1/16. The conglutination test revealed that clumping was present to a titre of 1/8. The serum agglutinated the red cells of all four donors and of six other Rh-positive specimens of blood at room temperature. There was no clumping of Rh-negative red cells. The serum of the four donors did not agglutinate the red cells of the patient. Fortunately serum taken from the patient before the blood transfusion was still available, and this was also sent to the institute for checking. The findings were as follows. Anti-Rh agglutinins were present to a titre of 1/32 (++), 1/64 (+), 1/128 (+). By direct matching the serum was compatible with the red cells of the four donors of blood group O (IV) at room temperature for 30 minutes. At 37°C . the cells of the donors were agglutinated. The titre was 1 (+).

The patient was apparently made sensitive to Rh-positive blood by the intramuscular injection of 20 millilitres of blood in January 1944, there being no history of previous blood therapy.

This case raises the point that, for the absolute safety of the patient, either one of the following two precautions should be taken if there is a history of previous blood transfusion or intramuscular injection of blood. (i) Their blood should be tested for the Rh factor, and if it is Rh-negative, they should be given Rh-negative blood. (ii) The cells of the donor's blood and the patient's serum should be incubated at 37°C . for twenty minutes before being pronounced compatible. The latter procedure, being the more practicable, is to be used at the hospital in all future cases in which there is a previous history of any blood therapy.

Prophylactic Use of Paludrine in a Tea Estate

By A. P. RAY

(Abstracted from the *Indian Journal of Malariology*, Vol. 2, March/June 1948, p. 35)

A CAREFULLY supervised field trial has been carried out, and from the results recorded it is concluded that:—

(i) Paludrine is an effective prophylactic and suppressive in both B.T. and M.T. malaria in a dose

of 0.3 gm. weekly, or 0.1 gm. twice weekly at spaced intervals.

(ii) Chloroquine is equally effective in doses of 0.25 gm. of base once weekly.

(iii) There was no toxicity observed with either drug.

Although attendance was improved as compared with previous years, no attempt is made to assess the economic gains to the employers or the employees.

Chloroquine (SN 7618) in Malaria

By R. N. CHAUDHURI, *et al.*

(Abstracted from the *Indian Journal of Malariology*, Vol. 2, March/June 1948, p. 1)

A REPORT on clinical trials with chloroquine (SN 7618) on 50 malaria cases is given. The therapeutic course is short; it is fairly well tolerated and brings the temperature to normal in an average period of 26.8 hours with regime 'A' and in 24.9 hours with regime 'B'. It clears the peripheral blood of asexual parasites in an average period of 35 hours with regime 'A' and 25.5 hours with regime 'B'. The number of patients treated with regime 'B' is however too small to be compared with regime 'A'. Taking both the regimes together the temperature became normal in an average period of 25.5 hours and asexual parasites disappeared from the blood in 33.3 hours. Although the series is rather small, these results have shown that the drug is effective in terminating and attack in a shorter time as compared with quinine, mepacrine or paludrine. Twenty per cent of the cases have so far relapsed. It has been reported that a single weekly dose of 0.25 gm. of chloroquine is sufficient to suppress malaria. If this is confirmed, this drug will prove more effective than mepacrine or paludrine, but from the practical point of view, we must consider that chloroquine is more expensive and has a toxic action which, though mild and temporary, occurred in 10 per cent of the cases. The gametocytes were apparently unaffected, but in those cases in which they were absent when the treatment was started, they frequently failed to appear subsequently.

The New British Pharmacopœia

(Abstracted from the *Medical Press*, Vol. 219, 19th May, 1948, p. 449)

THE new volume gives evidence of much learning and, as far as can be judged, is an accurate work of reference. It contains some 150 new substances and preparations. Thus there are over 50 new injections, 17 new tablets and a number of new vaccines. But the most surprising feature, perhaps, is that of the omissions. All the plasters are gone, together with such old-fashioned preparations as the confections, and crude drugs such as asafoetida and buchu and even cinchona. One looks rather anxiously for the quinine salts, the use of which in many cases has been disparaged of late, but they are mostly still official although we miss iron and quinine citrate and ammoniated tincture of quinine. Gone, or almost gone, are the fresh infusions, some of the pills and some syrups. We have long found Easton's syrup to be a most valuable tonic, although it is admittedly an unstable chemical preparation, and it now ceases to be official. Parish's syrup remains.

We welcome the many new chemical substances, the value of which has been or is being proved, but we feel that some notes of warning should be sounded. The very potency of these substances creates dangers and the way in which they are prescribed for use,

that is to say, chiefly in the form of tablets, the taking of which is fatally easy and often leads to abuse. These dangers should receive the attention of the Poisons Board and also of the Central Health Service Counsel which is about to be set up under the New National Health Act. Many of these substances should at least be added to, if they are not already in, the list of drugs of such potency that they can only be obtained by means of a prescription, the repeating of which should be strictly controlled. But even with these precautions there is further danger. We note in a paper just published from the Metropolitan Police Laboratory that drugs of the barbiturate group are increasingly found to be the cause of suicidal and accidental deaths, and forensic analysts find difficulty in proving which chemical of these groups has been used or abused. Again, the sulpha group of drugs consists of powerful substances which are either known by their chemical names (which are mysteries to the lay and even the medical mind) or specified by what can only be described as nicknames, consisting of initials and numerals.

The *British Pharmacopœia*, 1948, is being published for the General Medical Council by Constable and Co., Ltd., on 1st September, 1948, and will from that date supersede previous issues. The price will be announced nearer the publishing date.

Male Fertility

(Abstracted from the *Urologic and Cutaneous Review*, Vol. 51, August 1947, p. 481)

IN the evaluation of male fertility, states G. A. Humphreys (*Pennsylvania Medical Journal*, June 1947), what is necessary is (1) a history of the case, (2) physical examination, and (3) semen analysis. If the semen specimen is collected from a patient about a week after coitus, it will probably reflect his fecundity more accurately than if collected sooner.

In examining the specimen the following observations should be made:

(1) *Volume*.—The average specimen is around 3 cc.

(2) *Viscosity*.—It is important to determine this on a fresh specimen.

(3) *Motility*.—If we count 20 to 30 spermatozoa and note the number of motile and immotile, we can determine the percentage of active cells. These observations should be made at the end of four, eight, twelve, and twenty-four hours. In normal motility, the spermatozoa should be able to cross the high-powered field in a straight line with fair speed. Circular or retrograde motility is as abnormal as is initial sluggish movement.

(4) *Spermatozoa count per cc. and total*.—MacLeod and Hotchkiss considered 60 million per cc., a good dividing line between good and poor fertility.

(5) *Morphology*.—Abnormal morphology frequently accompanies.

GENERAL SUGGESTIONS

(a) When the volume of the ejaculated semen is small and the per cc. and total count somewhat subnormal, it is advisable to have the patient refrain from intercourse for about 10 days prior to the wife's fertile period in order to have his semen optimal at the crucial time.

(b) When the viscosity of the semen is poor, there may be marked improvement in a small percentage of cases following local treatment and chemotherapy. The wife should be kept in the Trendelenburg position for 8 hours following intercourse during the fertile period.

(c) When the motility is poor, the administration of a small daily dose of desiccated thyroid may improve the motility in some cases.

Spontaneous Hæmatomata of the Vulva

By J. H. HANNAN

(Abstracted from the *Medical Press*, Vol. 219,
31st March, 1948, p. 292)

SPONTANEOUS hæmatoma is a very uncommon complication of childbirth and fortunately so, since it is attended, with a very high mortality.

Spontaneous cases usually occur in normal deliveries where no instrumental interference has taken place, and are easily overlooked.

The following case illustrates this:—Mrs. B., aged 24, delivered herself naturally of a living male child, weight 7 lb. 11 oz., which appeared normal.

Twelve hours after the confinement, the woman appeared collapsed and had air-hunger. She had a fairly large hæmatoma of the vulva and was in extremis with all the signs of concealed hæmorrhage. The only sign of external hæmorrhage was a moderately sized hæmatoma of the left labium major. A transfusion of 3 pints group 4 blood was given, but in spite of this she died some 18 hours after delivery. At post mortem, a large retroperitoneal hæmatoma representing at least 3 pints of blood was found. No other abnormality was found in the genitalia, pelvic organs, or organs generally, with the exception of the labial hæmatoma which had spread through one side of the pelvis and was directly connected with the retroperitoneal hæmatoma.

The pathology of this condition is very vague. Some ascribe it to being due to condition similar to that of a male bleeder—true hæmophilia.

Yet no true hæmophilia in the female is possible. Others ascribe the condition as being allied to the purpuras, while others suggest that the cause lies in an increased fragility of the blood vessels, which rupture when the lining of the vaginal canal is stretched.

In view of the seriousness of the condition, the writer would suggest that all instances of spontaneous hæmatomata of the vulva should be treated with suspicion and energy.

The writer said that he should be tempted to open the hæmatoma in the next case, and after evacuation of the clot, he shall pack the cavity with gauze impregnated with snake venom.

The Use of Testosterone Propionate in the Treatment of Advanced Carcinoma of the Breast

(From the *Medical Press*, Vol. 218, 10th September, 1947, p. 230)

CARCINOMA of the breast is a problem to every practising doctor, and advanced cases are all too common.

Hermann, Adair and Woodward (*Surgery*, July 1947) of New York have described the results obtained by the use of testosterone propionate in the treatment of cases with osseous metastases from carcinoma of the breast.

The patients ranged in age from 39 to 62 years. With three exceptions they were treated exclusively with testosterone propionate administered intramuscularly. Symptomatic improvement, evident within two weeks after the institution of the therapy, was manifested in the majority of the patients. Many patients revealed x-ray evidence of calcification in the metastatic areas. In some instances as bone density increased there was a drop in the serum calcium indicating either a deposition of this element in the metastatic areas or a decrease in osteolysis. There was

a rise in the serum alkaline phosphatase in most patients.

The dosage employed successfully were 100 and 200 mg. bi-weekly and 100 mg. tri-weekly. The treatment was continued until the patient became asymptomatic.

From the results obtained by these investigators it would appear that testosterone propionate is of value in the treatment of osseous metastases secondary to carcinoma of the female breast.

Streptomycin

(Announcement by Ministry of Health)

(From the *Pharmaceutical Journal*, Vol. 159,
6th September, 1947, p. 160)

THE Ministry of Health states that preliminary results of the streptomycin trials organized by the Medical Research Council have proved sufficiently encouraging to justify the view that, as available supplies of the drug permit, patients suffering from tuberculous meningitis or military tuberculosis should be given the opportunity of receiving treatment with the drug. While streptomycin is the best drug at present available for the treatment of these conditions, it prolongs life and relieves symptoms in only a proportion of the cases, and it is too early to say yet whether it ever produces a permanent cure.

The production of streptomycin in Britain is still very limited; but additional supplies obtained from the United States of America have enabled arrangements to be made for a certain number of medical schools to receive an allocation each month for use in teaching or associated hospitals. The number of beds for which supplies are available at the moment in the United Kingdom is about 150. The cost of streptomycin is still very high, and for the time being the supplies are being distributed by Government to the medical schools free of charge. In view of the limited experience of treatment with streptomycin in other conditions, the medical schools have been asked for the present to restrict treatment with the drug to cases of tuberculous meningitis and military tuberculosis. It is not recommended for use in chronic pulmonary tuberculosis.

The following is a list of the hospitals in England and Wales and Northern Ireland at which cases of tuberculous meningitis and military tuberculosis will be treated with streptomycin:—

ENGLAND

Liverpool	.. Alder Hey Children's Hospital, Liverpool (6 children's beds). Royal Southern Hospital, Fazakerley (3 adult beds).
Sheffield	.. Children's Hospital, Western Bank, Sheffield 10.
Newcastle	.. Royal Victoria Infirmary, Newcastle.
Bristol	.. Bristol General Hospital, Bristol 1.
Manchester	.. Royal Infirmary, Manchester.
Birmingham	.. Children's Hospital, Ladywood Road, Birmingham 16.
Leeds	.. General Infirmary, Leeds. St. James' Hospital, Leeds.
London	.. Middlesex Hospital, W.1. St. Bartholomew's Hospital, E.C.1. London Hospital, E.1. St. Mary's Hospital, W.2. St. Thomas' Hospital, S.E.1. Guy's Hospital, S.E.1.

WALES

Cardiff	.. Cardiff Isolation Hospital.
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NORTHERN IRELAND

Belfast	.. The Whiteabbey Sanatorium, Whiteabbey, Belfast. Purdyburn Fever Hospital, Purdyburn, Belfast.
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Similar arrangements are being made in Scotland and details will be announced shortly.

Medical practitioners who have a case of suspected tuberculous meningitis or miliary tuberculosis are instructed to get into touch direct with the nearest convenient hospital on the list, or (in the case of hospitals in the London area) with the Emergency Bed Service (Monarch 8315). This scheme for the treatment of tuberculous meningitis and miliary tuberculosis does not in any way affect the arrangements already made by the Medical Research Council for the treatment in certain hospitals of cases of meningitis due to *Hæmophilus influenzae*.

A Contribution to the Ætiology, Diagnosis and Therapy of Pemphigus

By D. I. MACHT

and

M. OSTRO

(Abstracted from the *Urologic and Cutaneous Review*, Vol. 51, November 1947, p. 651)

ABOUT 25 years ago one of the authors conceived the idea of making comparative studies concerning the effect of drugs and chemicals on living plant protoplasm in contrast to living animal protoplasm. By pharmacology, as it is taught in most of our medical institutions, is meant a study of the effects of drugs and poisons on living animals. Strictly speaking, it is a zoopharmacology. However, just as the domain of physiology is subdivided into zoophysiology, or the physiology of animals, and phytophysiology, or plant physiology, so can the science of pharmacology be subdivided into zoopharmacology and phytopharmacology or study of the effects of drugs and poisons on living plants.

For practical pharmacologic purposes it was found that quantitative phytopharmacologic studies could be most conveniently made by measuring the root growth of certain seedlings reared in artificial plant-physiologic solutions. For such studies plant physiologists have found the seedlings of the *Lupinus albus* very useful, and the authors with their collaborators have employed them extensively in phytopharmacologic researches. These studies led to some very interesting findings which mark the beginning of a new branch of biology to which the name of *phytopharmacology* was applied. Perhaps the most fruitful results yielded by such studies was the discovery in the blood of various toxic substances which could not be demonstrated by zoopharmacologic methods, and not even by ordinary physical or chemical methods. In this way it was demonstrated scientifically that there is a toxic substance—menotoxin—present in the blood and other secretions of menstruating women. Another discovery was the presence of a specific toxic substance in the blood of pernicious anæmia which is not present in the blood obtained from all other forms of anæmia and of leukæmias. A good resume of these phytopharmacological studies has been published.

Perhaps the largest number of blood samples examined by phytopharmacological methods was that obtained by Macht and Pels from various skin diseases. These studies were begun over twenty years ago. They included blood specimens obtained from every available kind of skin disease, and the results obtained were of great interest both from the negative and positive standpoints. It was discovered that the blood sera from most dermatoses gave exactly the same quantitative results in regard to their effect on the root growth of lupinus seedlings, with three exceptions, as the sera obtained from hundreds of normal individuals. The exceptions were leprosy, trachoma,

and pemphigus. These three ailments yielded bloods which were markedly toxic for the root growth of lupinus albus seedlings in hydroponic solutions.

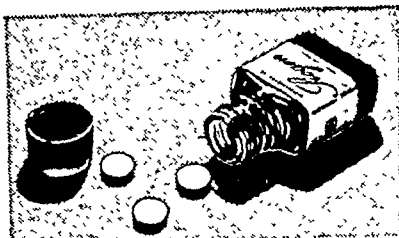
By far the largest number of cases studied in connection with these dermatological investigations were those of pemphigus. As early as 1927, it was discovered that blood sera of pemphigus patients contain a specific toxic substance which can be readily demonstrated by phytopharmacological methods based on *phytotoxic index* of growth. By the phototoxic index is meant the ratio of the root growth of lupinus albus seedlings in normal control solutions over a period of twenty-four hours in the dark at the temperature of 15°C., to the elongation of roots of other seedlings from the same crop grown in a 1 per cent solution of the unknown serum to be examined. Numerous studies by the above methods revealed that the sera of pemphigus gave phytotoxic indices ranging from 40 to 60 per cent. Table I gives the average figures obtained with pemphigus, leprosy, trachoma and a number of other dermatoses which may be mistaken for pemphigus and also the average readings obtained with normal blood sera as well as of other pathological conditions. All other skin diseases give normal readings.

TABLE I

Comparative toxicity of blood sera for *Lupinus albus*

Diagnosis	Index of growth or phytotoxic index, per cent
Normal individual ..	70-75
Menstruating individual ..	51-60
Pernicious anæmia ..	44-57
Pemphigus ..	40-60
Leprosy ..	47-50
Trachoma ..	47-60
Hodgkin's disease ..	60
Erythema multiforme ..	69-70
Erythema multiforme bullosum ..	70-75
Lupus erythematosus ..	70-75
Some toxico-dermatoses ..	60-65
Dermatitis herpetiformis ..	69-70
Senear-Usher syndrome ..	67-70
Mycosis fungoides ..	70-75
Sulphathiazole rashes ..	70-75
Penicillin in appreciable blood levels ..	60-65

The discovery that pemphigus blood sera after a brief exposure to filtered x-rays lose a large part of their phytotoxicity logically suggested a possible new approach to a rational treatment of pemphigus patients. What effect on the phytotoxicity of the blood would be produced by irradiating such patients? A priori the outlook appeared unpromising, for some years ago one of the authors showed that higher animals, including the human species, after treatment with x-rays exhibited toxic reactions of their blood within 24 hours after such treatment. Nevertheless, a trial of deep x-ray therapy in pemphigus patients was deemed worth while. The findings after the first such trials were both surprising and gratifying. It was found that brief irradiation of a pemphigus patient with doses 43 r. to 86 r. over the anterior hepatic and splenic regions reduced markedly the toxicity of the blood drawn 36 to 48 hours after treatment, for the lupinus albus seedlings. After two or three such treatments the phytotoxic index became normal (70 per cent to 75 per cent) and sometimes even higher than normal. Especially gratifying was the fact that as a sequence of the radiotherapeutic procedure and detoxification of the blood serum, the clinical condition of the few patients studied began slowly to improve; new crops of bullæ failed to appear; the old ones dried up, and the general condition of the patients became better.



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The VI Antigen in *B. typhosus*

By W. LEWIN

(Abstracted from the *South African Medical Journal*, Vol. 22, 22nd May, 1948, p. 338)

VI AGGLUTININS occur in the serum of a high proportion of chronic typhoid carriers, but these antibodies also occur in not inconsiderable proportions of the normal population, and cases of proved typhoid carriers are reported in whose serum Vi agglutinins cannot be demonstrated. Vi agglutinins may be produced non-specifically, as the work of Coleman has shown. The presence of *B. typhosus* Vi agglutinins in the serum of 'normal' persons may possibly be due to stimulation by a similar antigen present in organisms other than *B. typhosus*. The use of a prophylactic typhoid alcohol-killed alcohol-preserved vaccine will further limit the use of the Vi test in the detection of the carrier state. As long as all the factors related to the production and detection of Vi agglutinins in the serum of persons are borne in mind, the Vi test will continue to serve a useful purpose in the detection of carriers, but on no account should it be considered that the presence of Vi agglutinins in any titre in a serum is pathognomonic of the carrier state and their absence as indicating undoubted freedom from infection. Such a conclusion will, no doubt, be disturbing to medical officers of health, but it must be admitted that there is still no single absolutely reliable serological diagnostic measure for the detection of the typhoid carrier state. The isolation of the offending organism is still the only incontrovertible evidence of the carrier condition. What advice, then, are we to offer to public health authorities? Obviously, serological tests must be continued as a routine measure; by preventing all positive Vi reactors from handling milk and foodstuffs many typhoid carriers would be eliminated, but it must be realized that many 'normal' reactors would be penalized. Where finances permit, repeated bacteriological examination of faeces and urine should be undertaken. Carriers who do not exhibit agglutinins would be missed by serological tests, and because of this it is considered essential that milk, the common cause of extensive typhoid outbreaks, should be adequately pasteurized or boiled by the consumer. A great reduction in typhoid morbidity would occur if, in addition, large-scale prophylactic inoculation were carried out as is done amongst labourers on the Rand mines, where the morbidity rate has been reduced from 5.26 to 0.25 per thousand.

Reviews

WAR WOUNDS OF THE EXTREMITIES. WAR SURGERY SUPPLEMENT NO. 2 (BRITISH JOURNAL OF SURGERY).—Edited by H. J. Seddon. Published by John Wright and Sons Limited, Bristol. Price, 12s. 6d. Free to subscribers to the journal

This is the second of the war surgery supplements issued by the Editorial Committee of the *British Journal of Surgery*, the first one being on wounds of the head which was issued in 1947. In a stimulating foreword H. A. Thomas Fair-Bank briefly refers to the various factors that contributed to better results than those obtained in the first world war. One important development was the functioning of the mobile surgical units as close to the front line as circumstances permitted, so that the more severely wounded received attention at the earliest possible moment. Even paratroops were accompanied by a specially trained doctor who dropped to earth with his team and equipment and gave surgical treatment

to those in urgent need, in spite of the complete isolation of the Force. In some desperate cases transfusion was started at the Aid Post and continued in the ambulance as they travelled to the surgeon. On the whole, the lessons gained in the 1914-18 war, new developments in chemotherapy and the excellent team work produced a much higher standard of work.

The volume contains five reviews of wounds of the extremities written by specialists with wide experience and edited by H. J. Sedden embodying the experiences of war. The contents are: (a) war injuries of the extremities and their treatment in forward areas, (2) missile wounds involving bone, (3) early treatment of penetrating wounds of joints, (4) war injuries of peripheral nerves, and (5) war injuries of peripheral arteries. They are all of practical interest to surgeons in civilian practice, representing the modern methods of treatment in the various conditions described. The printing and illustrations are up to the standard of the journal. The third and fourth volumes will deal with abdomino-thoracic wounds and plastic surgery respectively.

R. N. C.

EMERGENCIES IN MEDICAL PRACTICE.—Edited by C. A. Birch, M.D., F.R.C.P. 1948. E. and S. Livingstone, Limited, Edinburgh. Pp. xi plus 468. Illustrated. Price, 25s. Postage, 9d. (home)

MANY problems which arise suddenly and unexpectedly in general practice have been answered in this valuable book. There are eighteen contributors, besides the editor, who have taken part in its preparation, presenting many practical informations. Management of acute (non-surgical) abdominal catastrophes by Dr. Birch, Dr. Rae Gilchrist's contribution on cardiovascular emergencies and Dr. Avery Jones's account of gastro-duodenal hæmorrhage are particularly good. Medical emergencies at sea and in the air have also been well dealt with. Other important heads are gynaecological and obstetrical, respiratory, neurological, psychiatric, renal, tropical, medico-legal and industrial emergencies. Certain conditions such as amenorrhœa, tuberculous salpingitis, polycythæmia, etc., are however seldom regarded as emergencies. The first chapter includes a list of contents of an emergency bag, but such essentials as ampoules of quinine and glass slides are lacking, while the last chapter deals with the common practical procedures. The volume is well produced on good quality paper and the illustrations are excellent. The book should find a valued place by the side of its surgical colleagues.

R. N. C.

THE SKIN DISEASES.—By James Marshall. 1948. Macmillan and Co., Ltd., St. Martin's Street, London, W.C.2. Pp. 363. Price, 30s. net

This medium-sized book is a masterpiece of compactness and clarity in skin lore.

The author has built dermatology round the manifestations of syphilis on the skin. This has specially appealed to the reviewer whose acquaintance with dermatology began in the same way. In the differential diagnosis of syphilis one must know something about all skin diseases.

Further, the author has shown amply that 'dermatology may not yet be a science but it is not a mystery'.

All the common diseases have been described fully in so short a compass that room has also been found for rare ones like Schamberg's disease, Bowen's disease, calcinosis cutis and amyloidosis cutis.

First 52 pages lay the foundation of anatomy and physiology of the skin, pathological changes in the skin, symptomatology of the skin diseases and principles of treatment (including prescriptions).

With the aid of this book every general practitioner should recognize a skin disease. For treatment he can go beyond the book, if necessary.

Some flaws inseparable from first edition attract attention : Page 52—Whitfield's Ointment, 3rd line is faulty; page 147—Corneal Scarring in the picture is not seen; page 191, line 19—grey scale sand crusts.

The get-up is good. The pictures though mostly in black and white are excellent. The price could be lower and the same as that of its companion volume **THE VENEREAL DISEASES**.

S. D. S. G.

THE VENEREAL DISEASES.—By James Marshall. 1948. Macmillan and Co., Ltd., St. Martin's Street, London, W.C.2. Pp. 369. Price, 21s. net

In the first edition of this book the author took special care 'to keep the practical problems to the fore'. They have been so kept in this edition also. The essential additions are penicillin treatment, Reiter's syndrome and massive arsenotherapy.

The book in spite of its small size contains many original observations. Random samples are : (1) Gonorrhoea in the male is usually contracted from a young woman of the amateur class. One reason is that the amateurs generally outnumber professionals. (2) Excessive coitus and prolonged amorous play can produce mucoid discharge, the one from the second cause being 'fiance's gleet'. (3) Persistently positive blood tests in an adult are evidence of syphilis even in the absence of clinical signs.

With the use of provocative injection in syphilis the reviewer is not in agreement in India. It provokes the non-specific reactions also. Incidentally, the list of non-specific conditions responsible for a false positive W.R. is not complete. The causative agent of granuloma inguinale is not a leishmania-like organism.

Rare venereal diseases are included, Peyronie's disease being one of them.

The practical instructions towards the end of the book are very helpful although the reviewer does not agree with 'the needle bevel face up'. This is the usual recommendation. The bevel should as a matter of fact be face down : otherwise the needle entering the vein in the direction of the heart carries down with it a flap and bends it in such a way that its convexity, later, meets the incoming blood. The flap cannot, therefore, be straightened automatically. When the bevel is face down the flap carried down is bent in such a way that its concavity meets the incoming blood. The flap, therefore, can be straightened automatically.

The get-up is good and price reasonable.

S. D. S. G.

THE AMERICAN ILLUSTRATED MEDICAL DICTIONARY.—By W. A. Newman Dorland, M.D., F.A.C.S. Twenty-first Edition. 1947. W. B. Saunders Company, Philadelphia and London. Pp. 1660. Price : Plain Edition, 40s.; Indexed Edition, 42s.

The present edition gives an accurate idea of the wealth of information the medical world is acquiring so rapidly and more or less unexpectedly. On page 582, for instance, between the words 'fundus' and 'fungate', which were consecutive in a previous edition, there are no less than four new words : funduscope, funduscopy, fundusotomy and fungal. These words are quite well established now and yet we never felt their want a few years ago.

Illustrations particularly those in colour deserve special mention, prominent among them being : 1. Anterior pituitary hormone, facing page 674. All that is known of the hormone can be grasped from the illustration almost at a glance. 2. Life cycle of the malarial parasite of man, facing page 1133. 'Probable tissue stages (cryptozoites)' have retrieved this excellent plate from obsolescence. 3. Diagram of autonomic nervous system, facing page 1447, again gives at a glance how we are governed. Pictures of men of

medicine and science bridge the gulf and the present, and bring the seeker face to face with expounder. Their artistic merit is of a very high order.

There are two useful indexes—index to the tables and index to the portraits—and a table of Greek alphabet which mathematically inclined medical men might appreciate particularly. Some copies also possess a thumb index which the reviewer's copy does not possess. This appears to have saved the publishers two shillings.

The lexicon fulfils its duty in debunking the top-heavy hæmatology. A monocyte, it says, 'includes large mononuclear leukocytes and transitional leukocytes'. So it does and is, therefore, not an exact term at all.

An item missed by the reviewer is the history and associated explanation of the metric system : how a cc. almost surreptitiously and quite unnecessarily has become a mil.

A word now omitted but previously given is Agnolin. It came before Agnosia.

The present edition keeps its high rank among the medical dictionaries. The get-up is excellent and price reasonable.

S. D. S. G.

A-B-C'S OF SULFONAMIDE AND ANTIBIOTIC THERAPY.—By P. H. Long, M.D., F.R.C.P. 1948. W. B. Saunders Company, Philadelphia and London. Pp. x plus 231. Price, 17s. 6d.

BASED on twelve years of experience at John Hopkins, the author presents the essence of the use of sulphonamides and antibiotics. The subject-matter is up to date, well-written and easy of reference since diseases are arranged alphabetically. The clinical pharmacology and toxicity and methods of administration are described in a practical manner. Only antibiotics of proved value have been included. The book will be useful to the general practitioners.

R. N. C.

AIDS TO PHYSICAL CHEMISTRY.—By R. G. Austin, B.Sc. (Lond.), F.R.I.C. Second Edition. 1948. Baillière, Tindall and Cox, London. Pp. xii plus 443 with 61 illustrations. Price, 7s. 6d.

It is an excellent book for beginners in physical chemistry specially for rapid revision purposes. Each chapter has been presented in a clear but concise way. The only important portion that has not been touched is thermodynamics. This is indeed a difficult subject for beginners but a short introduction into the subject would have been helpful to the students. This book will be found useful by pass B.Sc. and medical students of Indian universities.

R. C.

AIDS TO BIOCHEMISTRY.—By E. A. Cooper, D.Sc. (Lond.), F.R.I.C., A.R.C.S. (Lond.), and S. D. Nicholas, B.A. (Oxon.), A.R.I.C. Fourth Edition. 1948. Baillière, Tindall and Cox, London. Pp. viii plus 244 with 11 illustrations. Price, 5s.

ESSENTIALS of biochemistry have been neatly packed up inside a small volume. In spite of the compact size there is ample information regarding the detection and estimation of biochemical products. In this respect a few more words on the use of modern photo-electric colorimeters would have been welcome.

R. C.

BOOKS RECEIVED

1. Indian Engineering. Volume CXXIV, No. 6, December 1948. Printed and published by the Calcutta General Printing Co., Ltd., 300, Bow Bazar Street, Calcutta 12. Edited by F. W. Mennell.

2. Proceedings of the Society for the Study of Industrial Medicine. Volume I, No. 1, March 1949. Edited by Lieut.-Colonel Najib Khan. Published by Lieut.-Colonel Najib Khan, for the Society for the Study of Industrial Medicine, Jamshedpur.

3. Texas Cancer Bulletin. Sponsored by The Texas Cancer Co-ordinating Council. The State Medical Association of Texas, Cancer Committee. The Texas State Department of Health, The University of Texas, U.S.A. Published bi-monthly. September-October 1948 number.

4. Polski Tygodnik Lekarski. R. IV, Nos. 1, 2, 3 and 4. Warszawa, 3 stycznia 1949 r., Warszawa, 10 stycznia 1949 r., Warszawa, 17 stycznia 1949 r. and Warszawa, 24 stycznia 1949 r.

5. Chikitsa-Jagat. Vol. XX, No. 7, May 1949. Monthly medical journal. Written in Bengali. Edited and published by Dr. Amulyadhan Mukharji from 27C, Upper Circular Road, Calcutta 9.

Abstracts from Reports

ANNUAL REPORT OF THE DIRECTOR OF THE PASTEUR INSTITUTE OF SOUTHERN INDIA, COONOR, TOGETHER WITH THE FORTY-FIRST ANNUAL REPORT OF THE CENTRAL COMMITTEE OF THE PASTEUR INSTITUTE ASSOCIATION FOR THE YEAR 1947-48. PRINTED AT THE DIOCESAN PRESS, MADRAS

Antirabic treatment.—The antirabic vaccine employed for the treatment of human patients was a 5 per cent suspension of sheep brain (Paris strain of fixed virus) in carbol-saline prepared by Semple's method. A total of 3,054,224 cc. was manufactured during the year. During the year under review 18,166.5 courses of antirabic vaccine were issued.

During the disturbances in the Punjab when the Central Research Institute, Kasauli, could not supply antirabic vaccine, this Institute supplied at the instance of the Central Government 331,020 cc. of antirabic vaccine to the Government of United Provinces and the Dominion of Pakistan.

(a) Patients treated at the Pasteur Institute :—

During the year under review 323 patients received a complete course of antirabic treatment at the Institute (314 Asiatics and 9 Europeans). Incomplete courses of treatment were also given to 61 patients, of whom 29 were absolved from further treatment after the possibility of rabies in the biting animals had been excluded. The remainder absconded.

The subsequent history of treated patients was ascertained six months after the completion of treatment in 88.8 per cent cases.

One death was recorded among the 355 patients who received complete or incomplete courses of treatment giving a mortality rate of 0.29 per cent. The death occurred in an Asiatic patient.

Advice, but no treatment, was given to 208 persons.

During the 41-year period from 1907 to 1947, the total number of patients treated at the Institute was 40,776, among whom 403 subsequently died of rabies giving a mortality rate of 0.99 per cent.

(b) Patients treated at Subsidiary Centres :—

The various centres returned 13,930 case cards for patients treated during the year under review. Of these, 8,799 received a complete course of treatment and 4,849 were incompletely treated. Sixty-six patients were absolved from further treatment as the possibility of rabies in the biting animals was excluded. The remaining 216 were not taken into account for statistical purposes for want of sufficient details in the case cards.

Eleven deaths were recorded among the 13,648 patients who received complete or incomplete courses of treatment giving a mortality rate of 0.08 per cent.

The total number of patients treated at the Subsidiary Centres during the 26-year period from 1922 to 1947 was 217,280, among whom 727 deaths were reported giving a mortality rate of 0.33 per cent.

All the 11 deaths reported during the year occurred among Asiatic patients and followed dog-bite.

No case of post-treatment paralysis ('Paralytic accident') was reported during the year.

Antirabic treatment was also made available for the prophylactic treatment of animals. While it is advocated that dogs should be protected before they are exposed to infection, it is found in practice that treatment is comparatively seldom given until the animal is at risk. During the year 159,930 cc. of 5 per cent carbolized sheep-brain vaccine were issued for the treatment of animals, chiefly to Veterinary Officers of the Madras Presidency and the neighbouring Indian States. The number of animals treated during the year was 1,324 of which 855 were dogs.

General Laboratory Work

Routine laboratory examinations were carried out on a large scale for the benefit of hospitals, dispensaries and practitioners. The total number of examinations carried out during the year was 2,987. Most of this was done free of charge, but fees were recovered at scheduled rates from patients who were in a position to pay, except in the case of Government servants.

Blood Bank

The Blood Bank work at the Institute was continued. During the year 39,910 cc. of plasma were prepared. Since the inception of the Blood Bank in 1942, a total of 127,335 cc. of plasma have been prepared and issued to various civil, military and mission hospitals.

(i) RABIES

(a) Studies on the cultivation of rabies virus in vitro

Research work.—It has been reported that rabies virus can be cultivated in a cell-free medium containing 1.5 per cent steamed sheep-brain extract, 2 per cent sheep serum, 2.5 per cent glycine and 0.15 per cent peptone. With the addition of tryptophane and accessory factors like thiamine hydrochloride, pyridoxine hydrochloride, calcium pantothenate, nicotinic acid, riboflavin and biotin to the above medium, it was possible to step up the titre of the cultures to at least 500 million m.l.d. per ml. When tryptophane and all the above factors were added it was possible to dispense with the use of steamed sheep-brain extract in the medium. Concentrations as high as 5,000 million m.l.d. per ml. were obtained with a medium containing 2.5 per cent glycine, 0.15 per cent peptone, 2 per cent sheep serum, 2 mg. per cent tryptophane, 2 micrograms per ml. of each of thiamine hydrochloride, pyridoxine hydrochloride, calcium pantothenate, nicotinic acid and riboflavin together with 0.2 ml. per 100 ml. of a biotin concentrate. The concentration of virus obtained in cultures with the above medium was about 3,000 times that obtained in the brains of infected sheep used in the manufacture of antirabic vaccine.

Studies are in progress to determine whether it would be possible to eliminate peptone and serum from the medium by the substitution of certain amino acids.

(b) Studies on antirabic immunization with culture vaccine

A series of immunity experiments with culture vaccine has been carried out.

The results showed that, under the conditions of test employed, formalized culture vaccine and 5 per cent Semple's vaccine had little or no protective value while phenolized culture vaccine had considerable immunizing properties.

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Original Articles

REPORTING MALADIE DE ROGER AS A FAMILIAL CHARACTERISTIC IN FIVE MEMBERS OF A UNIQUE FAMILY

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and

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MALADIE DE ROGER or Patent Interventricular Septum, as a clinical and cardiovascular entity, needs no introduction to the majority of practising physicians.

In 1879, Roger, for the first time, gave a clinical description of this relatively asymptomatic cardiovascular entity; his lucid exposition of the physical signs of this disease remains unrivalled to this day. It was Dupré, however, who confirmed Roger's contention in the autopsy room in 1891 and gave the entity its present designation of 'maladie de Roger'.

In the opinion of Brown (1939), maladie de Roger is 'possibly the commonest of all congenital abnormalities' of the heart. This opinion is shared by one of us (R. J. V.), having noted this abnormality of the heart in well over a third of all cases examined for congenital diseases of the heart. Unfortunately, in view of the paucity of symptoms, the condition is likely to escape recognition. Diagnosis of maladie de Roger is usually established on the basis of certain well-recognized characteristics, viz (1) A peculiar absence of symptoms or subjective manifestations; this is indeed striking in the presence of such well-marked physical signs. (2) The presence of an 'almost pathognomonic' murmur, originally described by Roger as a 'long loud murmur'. This characteristic murmur, which occupies the whole of systole, is usually best heard in the third and fourth left inter-spaces close to the sternum and is accompanied by a thrill in about a third of the cases. (3) The absence of cyanosis and clubbing; occasionally, cyanosis does make its appearance as a delayed phenomenon, the so-called 'cyanose tardive'. (4) Radiologically, there is no distinctive cardiac contour, although the heart shadow often assumes a rather 'globular contour'; another feature worth noting is the prominence of the pulmonary artery. (5) The

electrocardiogram, being usually within the limits of a normal pattern, is not of much assistance in diagnosis, except perhaps from a negative aspect. (6) The association, although infrequent, of certain defects of conduction such as complete heart-block, with this congenital anomaly, is now a recognized fact.

Hereditary or familial tendencies have been reported from time to time in connection with various congenital cardiac abnormalities. Abbott (1927), for instance, reported cardiac anomalies 'in a brother or sister of the patient' in eleven of her cases. Brown (1939), was able to report a similar occurrence, in a brother or sister, in six of his series of cases of congenital heart disease. The maladie de Roger was reported in a mother and her child by Debre and others (1923). Seitz and Baumann (1935) were able to report septal defects in a father and four children.

The present report is rather unique in that it records the occurrence of as many as five cases of maladie de Roger in a single family, observed over two generations. The family came to our notice, by accident, during a routine consultation.

The accompanying *diagram* illustrates, at a glance, the salient features of this interesting family tree.

It will be observed from the diagram that out of the seven daughters of Mr. and Mrs. M. F. B., who are incidentally both free of congenital cardiac anomalies, two daughters (viz Mrs. J. H. K. and Mrs. K. R. D.) display the maladie de Roger, Mrs. J. H. K. happens to have eight children, all males, of whom one (viz Master M. H. K.) displays typical signs of maladie de Roger. The other sister, Mrs. K. R. D., with the cardiac anomaly has three children, of whom two (viz Miss S. R. D. and Master P. R. D.) display the maladie de Roger. In all, therefore, there are five clear-cut instances of maladie de Roger in this Parsee family of two generations. The physical signs

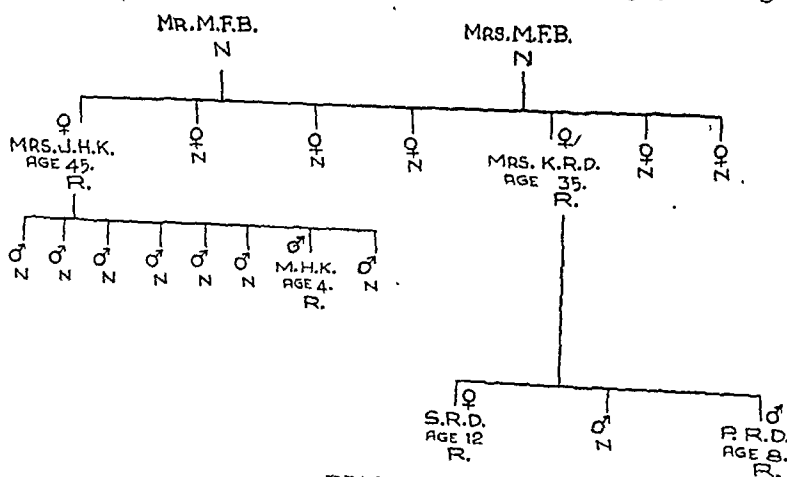


DIAGRAM.

The sign N in this diagram denotes a normal cardiovascular system; the sign R denotes the existence of a congenital cardiovascular anomaly of the nature of maladie de Roger.

in all these five cases are identical and conform closely to the classical descriptions of the disease.

Summary

The present report deals with a unique Parsee family, studied in Bombay, five of whose members (within two generations) display the classical characteristics of *maladie de Roger* or patent interventricular septum.

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SYMMETRICAL GANGRENE

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SYMMETRICAL gangrene is a condition in which gangrene occurs in all four limbs, the nose and ears at the same time. This is a rare condition and only very few cases have been recorded. A number of conditions can cause symmetrical gangrene. These areas, i.e. the limbs, the ears and the nose, represent the outposts of the cardiovascular system. When the body needs to conserve, it conserves at the expense of the outposts maintaining the circulation for the heart, the central nervous system, respiratory system and the splanchnic areas. Symmetrical gangrene may be attributed to diabetes, arteriosclerosis or thromboangiitis obliterans. It is also met with in ergot poisoning. As a result of acute infectious fevers like typhoid, typhus and malaria, it might also occur. Page has recorded a case of symmetrical gangrene due to vitamin-B deficiency. A few cases of symmetrical gangrene have been recorded in the Africans, but in the two cases described by Michael (1947) the gangrene was confined to the legs. In this country, Raynaud's disease is not likely to be an important condition. In the African series, it was noted that the disease occurred in persons who were previously in a good state of health. All of them occurred in men. The age incidence was between 20 and 35. It started with œdema of the legs followed by pain. Gangrene occurred in both legs simultaneously. No obvious cause was detected. In contrast to this series is the

case I am reporting, and which occurred in a woman of about 25 years of age.

Case report.—Mrs. R., Hindu, aged 25 years, was admitted on the 25th January, 1945, with the complaint of pain, œdema and discoloration of legs up to the middle including feet, and of nose and palms, said to be of one day's duration. The illness started with sudden fever and rigor about 15 days previously. This continued in the evenings of alternate days for 8 days. On the 11th day of onset, she noticed œdema of the feet and legs with severe pain. Red patches appeared subsequently on toes, fingers and, later, on the nose. The nails showed a blue tinge. The palms of the hands and left ear lobule were later affected.

Previous illness.—About a year ago, the patient noticed white discharge per urethra. This ceased after a few days. **Habits:** Non-vegetarian. **Family history:** She had two children. One died soon after birth and the other survived 3 months.

Condition on admission.—The patient looked about 40 years of age. She was very pale, and the skin was cold.

Lesions.—There was gangrene of hands and finger, lower limbs up to the middle of legs, nose and the adjoining part of the upper lip and lobule of the left ear. The thumbs were not involved. The nose was foul-smelling. The affected parts were œdematous, cold and tender and without any sensation to touch. There was a well-marked differentiation of the affected tissue from the normal. Pulsation was felt in the radial, but not in the dorsalis pedis and posterior tibial arteries.

Cardiovascular system.—Apex beat visible in the 5th space in the mid-clavicular line. It was forcible and rapid. Boundaries were normal. Sounds were well heard. No adventitious sounds. Pulse rate 120 per minute. Volume and tension good. Blood pressure 120/60.

Urine.—Specific gravity 1015. R.B.C.s ++; pus cells ++, phosphates ++. No sugar; no albumin.

Blood.—No malarial parasite. W.B.C. 7,200. P 64 per cent, L 26 per cent, M 8 per cent, E 2 per cent. R.B.C. 1.75 millions. Hæmoglobin 40 per cent. Blood, Kahn positive, W.R. strongly positive. Other systems normal.

After her general condition got better, amputation at the seat of election was done in all four extremities.

Discussion.—In this case the œdema which occurred in the limbs was similar to the œdema that had been observed in the African series. As Gelfand says, it was difficult to explain the œdema. In this case fever occurred first. For 8 days she had been without any treatment and for two or three days she had taken a medicine which she described as very bitter, probably quinine, but it is not certain that it was quinine.

She was a subject of syphilis as shown by Kahn and W.R. tests. The question as to whether quinine precipitated gangrene in a syphilitic individual has to be borne in mind, since either of them by itself can cause gangrene. In this case ergot poisoning does not enter the picture at all, since she never had any ergot given to her. In addition no nervous symptoms were noted and also the process would have been much slower, taking some weeks and not a matter of days as in this case. Burger's disease usually occurs in the younger age group as in this one, but intermittent claudication in the limbs is a precursor for some months and also the gangrene is more prominent in one limb or occurs only in one limb to start with, and it might have taken some months or years for the limbs to have been affected.

There is a rare form of symmetrical gangrene recorded by Fishberg (1940) caused by a clot blocking auriculo-ventricular valve on the left side. In this condition shock is a prominent feature; and attendant with the shock is the symmetrical gangrene. Lewis (1936) has recorded two interesting forms of symmetrical gangrene. The first group occurs in children or young adults with no previous history of vascular disease. At the time of onset, malnutrition or some other cause of chronic ill health may be present, or the onset may be sudden without any warning and several fingers and the toes may be affected. The main arteries are not obstructed. Lewis considers that there is damage to the intimal coats of the digital arteries which result in thrombosis. In this case, however, there is a preceding history of fever, pain and oedema in the affected areas and the gangrene has extended well above the toes and fingers, so that the damage to the arteries is more than digital. In the second group, described by Lewis, bilateral gangrene occurs in the elderly and is associated with diseases like cancer, tuberculosis or diabetes mellitus. The gangrene is often associated with much pain.

Vitamin deficiency diseases like pellagra, ariboflavinosis, hypoproteinæmia and other causes of malnutrition are unlikely causes in this case. These malnutrition cases have been found to exhibit thickening of the arteries and gangrene of the toes. These patients complain of pain for a long time. In the case reported, I feel that the symmetrical gangrene was due to a syphilitic process having caused endarteritic changes in the peripheral vessels to which was added vascular spasm possibly through the action of quinine.

Summary.—A case of symmetrical gangrene is recorded in a syphilitic subject, the gangrene occurring in all four limbs and nose and the upper lip. Other causes for symmetrical gangrene are discussed.

My thanks are due to Lieut.-Colonel Sangham Lal, Superintendent, Government General

Hospital, Madras, for having permitted me to report this case.

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[W.R. and Kahn, by themselves, in a febrile disease may not establish a diagnosis of syphilis.—Editor, *J.M.G.*]

SYPHILITIC MANIFESTATIONS IN THE ORAL CAVITY

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THE clinical manifestations of the oral lesions are numerous each having their own peculiarities. The Dental-Surgeon should be familiar with the various stages of manifestation of the disease for his own protection, for the good of his patients and the safety of the society. Since the oral lesions may be present in all stages of the disease and since they are second in frequency to the genital lesions, the dentist has an usual opportunity for diagnosing unsuspected cases. The recognition of these extragenital syphilitic lesions is of particular importance, as the clinical appearance and symptomatology differ considerably from the genital lesions.

Site and appearance.—According to Doctors Wile and Holman of U.S.A. who made extensive study in extragenital syphilis, 57 per cent of the extragenital chancres are found on the lips, lower being more common. Next in order come oral mucosa, tongue, soft palate, tonsillar and pharyngeal region and rarely gums. Chancres of the oral cavity do not present the typical painless, brown, crusted, indurated lesion found on the genitalia because of the moisture, the trauma and bacterial flora present in the mouth. Chancres of the mouth are very often slightly painful and they are covered with greyish-white slough. Extra-oral lip chancres generally give typical characteristics, e.g. brown crusted appearance, while the intra-oral portion will have the greyish-white surface. Induration of the underlying tissues is not a prominent symptom as on other body surface. Herpetic lesions of the lips are often a problem in diagnosis. The superficial crusting which occurs following the rupture of a large vessel or a group of small

vessels simulates chancre. The persistence of the lesion, the regional adenopathy and dark-field examination will establish the diagnosis. Oral chancres are less painful than oral herpetic lesions, and they are not preceded by symptoms of burning and itching. The encrusted surface of a herpetic lesion is usually yellow in contrast with the brownish black of the chancre. The duration is short and frequently associated with an upper respiratory infection. The angle of the mouth is a frequent site, and in this location the lesions present a split or folded appearance caused by the folding of the tissue.

Oral mucous patches are often mistaken for fusospirochaetal ulcerations or traumatic lesions. The fusospirochaetal ulcerations are more acutely painful and typical gingival lesions are found. The syphilitic lesions have a translucent appearance and are oval in shape. Darkfield and blood Wassermann will confirm the diagnosis. Mucous patches are frequently observed on the tongue, the partial loss of the lingual papillae over the lesions clearly demarcates them from the uninvolved tissue.

A case is recorded. Miss M.S., age 25 years, Anglo-Indian girl, was referred to me by her doctor for the diagnosis and treatment of a shallow developing ulcer which was noticed 2 weeks after she had her upper right 2nd molar extracted by her dentist. On casual examination I found the 'ulcer' was slightly painful, roundish in size with a tendency to spread towards the palate. Adenopathy was present. Lips, tongue and angle of the mouth normal. Questioning revealed no exposure. The girl's story was that at the time of extraction the dentist gave 'too many' injections as the tooth was strong. Up to about 2 weeks after extraction there was no complaint, the healing was normal, but after 15 days this 'ulcer' developed at the alveolus and spread gradually towards the palate. The dentist was immediately consulted who treated the area for fusospirochaetal infection. Repeated application of mild caustic was also done but to no effect. On further examination the lesion in question did not appear to me to present the typical clinical characteristics of either a fusospirochaetal ulceration or of a chancre. It was shallow and greyish white and not particularly painful on palpation. It rather looked more like an erosion than an ulcer. Erythema of the surrounding area or induration was absent. I sent the patient for blood Wassermann and darkfield examination of the superficial lesion; but both were negative. Smear stained in the usual way also revealed nothing. All these tests took about a week. During this week I only kept the patient on an antiseptic mouth wash. The ulcer showed signs of getting little bigger, and the patient of getting disgusted with expenses and no relief. Ultimately blood Wassermann and darkfield examination of material aspirated from the alveolus was done and found to be strongly positive. Questioning

revealed an interesting fact. The patient was a sexual pervert and 10 days following extraction she had buccogenital contact. Within 2 weeks of antiluetic treatment marked regression of the local lesion was noted.

Syphilitic gummata : (1) *On tongue*.—They are not unusual in the late untreated syphilis. Single gummas are often noticed on the dorsum of the tongue. When ulcerated their diagnosis is often a problem as malignant growth and tuberculosis often have similar appearance. Serology may be negative at this stage, so biopsy is indicated. Several smallish gummata may form in the tongue, during the time of healing, a series of nodules, scars and sulci are formed on the dorsum aspect often giving the upholstered appearance. The tongue looks distorted from fibrous texture and loss of covering papillae.

(2) *On palate*.—They are also observed in the late stage of syphilis not treated at all or improperly treated. Gummatous destruction of the palatal bone is the most frequent cause of pathologic palatal defects. In active gumma of the palate the marginal bluish colour is typical. While epithelioma and Vincent's angina may cause destructive changes of the palate, a perforation that does not show neoplastic changes on gross inspection is almost invariably syphilitic in origin.

Tabes dorsalis.—It is a late manifestation of the untreated or inadequately treated syphilis and may involve the mouth. It occurs 15 to 20 years after the initial infection. The individual experiences terrible pain radiating from one point or darts from one point to another. They are often a headache to many practitioners because of the perplexing character. Below is a very interesting case.

A case is recorded. Mr. S. S., aged 54, very wealthy man, was referred to me for his agonizing pain in the jaw. A note of the history and laboratory and x-ray findings were also supplied by the doctor. General health: Good build and apparently looks healthy. Blood Wassermann negative. Urine normal.

Blood pressure systolic normal, diastolic slightly sub-normal. X-ray of the head, normal. Antrum, normal both sides.

The patient complained of burning and stabbing pain which started from upper left 2nd molar region and spread towards the head and neck. The history of the pain was of one and a half years' duration. By this time he had 11 of his teeth extracted by different dental-surgeons, but with no relief. He has also severe pain in abdomen accompanied by nausea and vomiting.

This abdominal pain was at first suspected to be of gastric origin and was treated as such. When no benefit was observed the stomach, etc., were x-rayed and no abnormalities were noticed. This line of treatment was given up, specially when it was found that following the acute painful episode the patient got relief. The patient

was then treated as a case of trigeminal neuralgia, culminating in alcohol (75 per cent) injection into the left Gasserian ganglion from outside. The patient was better for about 3 to 4 months; but keratitis of the left eye followed, and after some time the eye was completely lost. Pain also recurred after four and a half months only. Questioning revealed history of luetic infection 20 years previously, which was successfully treated. The pain was more severe at night than during the day, and this kept the patient in terrible agony. The doctor's report stated that all sorts of known sedatives and hypnotic drugs had been tried, which only gave temporary respite during the night.

Oral examination by the writer revealed that the patient was almost edentulous except two upper central incisors. Wore quite good fitting full denture. Certain amount of paresthesias present in lip, tongue and cheeks. Following interesting facts were also noted: (1) Tenderness of the masseter and temporal muscles. (2) Death of the dental pulp of the upper two central incisors, without any history of trauma. (3) Intra-oral film of the upper left 2nd molar site showed slight necrosis of the alveolar process without any observable cause.

On the basis of these observations, the writer sent back the patient for spinal Wassermann, which was strongly positive. It is interesting to note that the patient responded surprisingly well to a few antiluetic injections.

Prenatal syphilis.—The oral changes associated with such cases represent at times the only visual symptoms of the infection and the dentist may be the first to suspect the disease. They include: (1) The rhagadic scarring about the mouth. (2) The changes in the teeth. (3) Other dentofacial abnormalities.

(1) **Syphilitic rhagades.**—These are linear markings that are found about the oral orifices. The acute lesion appears as a copper-coloured linear area covered with necrotic crust. They are more common on the lower lips because of the thinness of the epithelium covering the structure and its greater mobility.

(2) **Changes in the teeth.**—Hutchinson's triad: Dental changes of syphilis appear only in the permanent teeth. This triad includes dental hypoplasia of the permanent incisors. They are pegged, notched and widely spaced. There is general constriction of the crown towards the incisal edge. There is also rounding of the mesial and distal marginal ridges. Another characteristic defect is the 'mulberry' maxillary first molar. In this the cusps of the first molar are more centrally placed than those of the premolars, giving the molar a bud-shaped appearance on the occlusal surface, and striking defects are present in the grooves and fissures of the tooth. There is considerable speculation whether the dental defects mentioned above are the direct result of the *T. pallidum* in the enamel organ or whether they represent a

general interference with the function of the ameloblasts. Professor Gottlieb of Vienna has demonstrated the presence of *T. pallidum* in the enamel organ of developing tooth. These dental changes must be distinguished from those associated with rachitis or the exanthematous fevers. While there may be marked local areas of hypoplasia of the enamel and dentin, a constriction of the crown of the teeth or the cusps is rarely seen without a prenatal luetic infection.

(3) **Dentofacial changes.**—Malocclusion is commonly observed in prenatal luetics. 'Open bite' is very common. These deformities apparently result from a lack of development of the premaxilla, but this should not be a basis of diagnosis, other stigmata associated with it will be of diagnostic value.

A STUDY IN BENGAL AND BEHAREE FEMALE PELVIS BY ROENTGEN-PELVIMETRIC METHOD

A PRELIMINARY COMMUNICATION

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Introduction

IMPORTANCE of pelvic factor in labour needs no fresh emphasis. Modern work shows that besides the size of the pelvis, other factors, like its shape and midpelvic capacity, greatly influence the mechanism of labour. New classifications depending on the pelvic inlet, shape and other morphological features have been adopted by various authors. Very little has been done in India to enlighten the obstetricians about this very important factor of labour. In fact, the ideas on the female pelvis in this country are very vague and meagre.

Radiology has helped a lot towards this knowledge about the architecture of pelvis. All modern workers have taken its help in some form or other. Unfortunately, it has not been utilized in this country as yet and there is no record up till now of a systematic study of Indian female pelvis on modern lines. This work has therefore been undertaken with the object of getting a clear idea about the size of the pelvic inlet, shape of the pelvis and also to get an approximate idea about the midpelvic capacity by determining the relative width between the ischial spines as seen through the pelvic inlet. An attempt has also been made to evaluate the importance of external or clinical pelvimetry and to determine how far the shape of the pelvis influences the course of labour.

There are two reasons for the selection of the Bengalee and Beharee pelvis for this study. One is the situation of the hospital. It is on the boundary between the provinces of Bengal

and Bihar and as such the clinical material is derived mainly from these two provinces. The other is the population of the Indian sub-continent which is heterogeneous in nature. The morphology of female pelvis differs from race to race and it is presumably different in different parts of India. On the other hand, it is likely to be more akin in neighbouring provinces and it is thought that better results, more useful to the population under study, can be obtained if it is done regionally among a relatively homogeneous race living in a particular portion of the sub-continent. At the same time it is hoped that similar studies would be started in different parts of the country to study the problems regionally and ultimately giving a broader picture of Indian female pelvis.

Review of literature

The external pelvic measurements of Indian women had been studied from time to time by Lane (1903), Leicester (1907), Das (1918) and De Sa (1933). Das gave the following figures :—

Interspinous 21 cm.; intercrystal 24.8 cm.; introchanteric 27.0 cm.; external conjugate 17.5 cm.

Pan (1929) measured the dry pelvis of 64 Hindu women and concluded that compared with the British and American pelvises the average measurements of Hindu pelvis are about 1 cm. less. His studies were made exclusively on the internal diameters of the true pelvis—its inlet, cavity and outlet. He measured the conjugate vera as equal to 10.10 cm.

Das and his associates (1937) studied 93 dried pelvises of the Bengalee women with a view to determining the external pelvic measurements and true conjugate. They concluded that the Bengalee pelvis is smaller in comparison with other races excepting Andamanese and Australian natives so far as external pelvic measurements are concerned. They noted that there exists a marked correlation between the introchanteric diameter and true conjugate. Their measurements are as follows :—

Interspinous 8.20 inches (20.83 cm.); intercrystal 9.75 inches (24.76 cm.); introchanteric 10.67 inches (27.10 cm.); external conjugate 6.87 inches (17.45 cm.); true conjugate 3.81 inches (9.68 cm.).

Caldwell, Moloy and D'Esopo (1934, 1935) in a number of important papers stressed the fact that not only the size, but also the shape of the pelvis is important. They studied female pelvis radiologically and classified them into five parent types according to the shape of the pelvic inlet. These are : (a) gynæcoid or round brimmed pelvis, (b) android or wedge-shaped brimmed pelvis, (c) anthropoid or narrow brimmed pelvis, (d) platypelloid or flat brimmed pelvis, and (e) asymmetrical, or irregular brimmed pelvis. Besides these parent

types, many subvarieties and combinations are recognized; some 30 in all. Caldwell and his co-workers (1934, 1935), however, described five mixed types; the anthropoid-gynæcoid, the gynæcoid-flat, the android-anthropoid, the android-flat, and the android-gynæcoid. These authors believe that the shape of the pelvic inlet has a great influence on the mechanism of labour and engagement of the foetal head in cephalic presentation. The brim shape is also associated with certain other characteristics in the cavity and outlet of the pelvis.

Thoms also studied pelvises of American women radiologically and used somewhat different classification. Torpin (1948) has laid importance on the ischial spines and the relative width between them as seen through the pelvic inlet. The latter is of importance as it gives an idea of the midpelvic capacity. Its narrowing is of greater importance in those types where the whole pelvic cavity is relatively narrow as in anthropoid and android pelvis. In consideration of the midpelvic space, the architecture of the sacrum, splay of the sidewalls of the pelvis and subpubic angle should also be considered.

In this study altogether 60 pelvises have been examined up till now. Out of these, 41 patients have been confined in the hospital and their labour carefully studied. History of previous labours in multipara was also noted.

Technique

In this series radiological pelvimetry was done during puerperium usually on the 4th or 5th day. Direct roentgenpelvimetry by the pelvic inlet grid method and lateral soft tissue technique of Thoms and Torpin have been utilized throughout this study. For this patient's position is adjusted with the help of a suitable back rest to bring the pelvic brim parallel to the x-ray film and exposure is given using the Potter-Bucky diaphragm. Tube-film distance is 32 inches and exposure coefficients are 80 K.V., 50 milliamperes for 5 to 6 seconds. A 5-inch cone is used and the tube is centered on the centre of the pelvic inlet. On this picture is superimposed the shadow of a perforated plate where perforations are placed at a distance of $\frac{1}{2}$ inch from each other. The plate is placed at a height where the pelvic brim was originally situated so that they are equally magnified and direct readings are taken in inches. A lateral picture is taken to see the pelvis from side, particularly with a view to studying the sacrum, sacrosciatic notch, lumbar spine, inclination of the pelvic brim and sacrum to the horizon. For this the patient's position is adjusted carefully and the tube is centered on the sacrosciatic notch. Potter-Bucky diaphragm is used and the exposure coefficient is determined according to individual requirements.

Although this technique will not allow direct measurement of the dimensions of the pelvic cavity and outlet, it will enable one to get an

approximate idea regarding these by studying the relative width between the ischial spines, sacrum and its curvature, depth of the posterior pelvis, splay of the pelvic sidewalls, sacrosciatic notches and inclination of the sacrum to the horizon. These have been studied with a view to getting a general idea about the architecture and capacity of the pelvis as a whole. In this preliminary report more emphasis has been laid on the features of the inlet of the true pelvis.

Interpretation

While conscious of the fact that many pelves are more or less mixed in character, they are classified according to their dominant feature as determined by general look of the contour of the pelvic inlet, sacrum, sacrosciatic notches, etc. The following rules as enunciated by Williams have been followed in the classification with slight modification.

(a) *Anthropoid pelvis*.—The anteroposterior diameter of the inlet is long and the transverse diameter is relatively (or absolutely) short. The forepelvis may be average or narrow. The widest transverse diameter at the inlet is well forward and hence there is a wide sacrosciatic notch. The sacrum is long and narrow and may have six segments ('assimilation pelvis'). The inclination of the pelvis is very steep.

(b) *Gynaecoid pelvis*.—Well-curved rounded pelvis with anteroposterior diameter of the inlet less than the transverse by an inch of 2.5 cm. or less. The widest transverse diameter is well forward and the forepelvis wide and smooth. The sacrosciatic notch is from average to wide and the sacrum slopes backwards.

(c) *Platypelloid or flat pelvis*.—The anteroposterior diameter of the inlet is short and the transverse long. In this series a pelvis where the general outline of the inlet is flattened anteroposteriorly and the transverse diameter exceeds anteroposterior by more than one inch or 2.5 cm. has been taken as flat type. The widest transverse diameter in this lies approximately midway between the sacral promontory and symphysis pubis. The sacrum is small.

(d) *Android pelvis*.—Inlet is typically wedge shaped with the apex of the wedge at the symphysis. Forepelvis is narrow and funnel shaped. Anteroposterior diameter is shorter than the transverse by one inch or less. The widest diameter (transverse) is near the promontory. The sacrosciatic notches are narrow. Pubic rami are strong and thick.

Results

The results of the investigation have been divided into four parts.

Part I deals with determination of the type of the pelvis and its classification according to that of Caldwell and his co-workers (1934,

1935). Sixty pelves have been studied with this object and the results are given in table I.

TABLE I

Type of pelvis	Number of cases	Percentage	Caldwell and Moloy's series, per cent
Gynaecoid ..	31	51.7	50.6
Android ..	15	25.0	22.4
Anthropoid ..	6	10.0	4.4
Platypelloid ..	3	5.0	22.7
Asymmetrical ..	5	8.3	1.8

Comment.—When compared with the figures of Caldwell and Moloy (1933, 1938) who studied 215 pelves in the White and Negro races, it will be seen that there is a greater incidence of android and asymmetrical types in the present series. On the other hand, there is a lower incidence of anthropoid type. In the asymmetrical group the irregularity was mostly of a very minor degree, one-half being less developed than the other. Out of the five only one was really very irregular, being a Naegele's pelvis.

Part II deals with the measurement of the diameters of the pelvic inlet, namely conjugata vera, transverse diameter, posterior sagittal. Measurement of the relative width between the ischial spines is also dealt with in this part. Number of pelves studied for these purposes are sixty.

A.—Conjugata vera : Arithmetic mean—4.168 inches (10.42 cm.).

B.—Transverse diameter : Arithmetic mean—4.64 inches (11.60 cm.).

Measured in different types of pelvis, conjugata vera, transverse diameter of the inlet and posterior sagittal are given in table II.

TABLE II

Type of pelvis	Conjugata vera in inches	Transverse diameter in inches	Post. sagt. in inches
Gynaecoid ..	4.3	4.65	1.73
Android ..	4.32	4.66	1.68
Platypelloid ..	3.30	4.63	1.35
Anthropoid ..	4.88	4.62	2.11

Table III compares the figures of the present series with those for the white women presented by Williams (Bourne and Williams, 1945).

Comment.—Average diameters of the pelvic inlet in the present series are smaller than those for the white women. Average difference of conjugata vera is about 0.5 centimetre. Transverse diameter in the white women is relatively longer and the average difference between the two is 1.9 centimetres. In other words, the pelves in the present series are relatively

TABLE III

Type of pelvis	CONJUGATA VERA IN CENTIMETRES		TRANSVERSE DIAMETER IN CENTIMETRES	
	White	Indian	White	Indian
Gynæcoid ..	10.8	10.75	13.7	11.62
Android ..	10.5	10.80	13.5	11.65
Platypelloid ..	8.5	8.25	14.4	11.57
Anthropoid ..	11.7	12.20	12.9	11.55
Average ..	10.9	10.42	13.5	11.60

rounder in shape approaching more or less the type which Thoms (1941) called mesatipellic.

Relative distance between the ischial spines has been studied 53 pelves of different types and the results are tabulated in table IV.

A.—External conjugate: Arithmetic mean—7.16 inches (17.90 cm.).

Interspinous: Arithmetic mean—8.50 inches (21.25 cm.).

Intercristal: Arithmetic mean—9.60 inches (24.00 cm.).

B.—Difference between external conjugate and conjugata vera: Mean difference—3.17 inches (7.92 cm.). Range—2.6 inches to 4.3 inches (6.5 to 10.75 cm.).

Comment.—It has been found that in 32.5 per cent of cases this difference between external conjugate and conjugata vera lies below 3 inches or 7.5 cm. In another 50 per cent it is between 3 inches and 3.5 inches. In the rest, i.e. 17.5 per cent, it is above 3.5 inches.

Importance of external conjugate.—For European pelves, Baudelocque stated that by

TABLE IV

Type of pelvis	Number of cases	R.W.S.				MEAN R.W.S.	
		Between 3.0 and 3.4 inches		Between 3.5 and 3.9 inches		Inches	Centimetres
		Number of cases	Percentage	Number of cases	Percentage		
Gynæcoid ..	31	8	25.0	23	74.2	3.56	8.9
Android ..	14	6	42.9	8	57.1	3.48	8.7
Platypelloid ..	3	1	33.3	2	66.7	3.50	8.75
Anthropoid ..	5	3	60.0	2	40.0	3.3	8.25
Average ..	53	3.46	8.65

Comment.—Average relative width between the ischial spines (R.W.S.) is smaller than the corresponding figure in the white women. While the average in the present series is 3.46 inches or 8.65 cm., that between 3.5 inches and 3.9 inches should be considered as a favourable range. When it is above 3.7 inches, it may be said that the space in the midpelvic cavity is good. Table IV will show that a relatively greater percentage of gynæcoid and platypelloid pelvis has got a favourable range of R.W.S., i.e. has a fairly spacious midpelvis. It is smallest in the anthropoid type. Android type lies midway between gynæcoid and platypelloid types although its inlet measurements are almost similar to that of gynæcoid. From this it appears that there is likely to be greater difficulty in midpelvis in the anthropoid and android types than in the gynæcoid and platypelloid varieties unless compensatory spaces make up for this deficiency. This is in conformity with the conclusions of Caldwell and his co-workers (1934, 1935) and Torpin (1948).

Part III deals with external pelvic measurements and the relationship with the inlet diameters as determined by roentgenpelvimetric method. Sixty pelves have been studied in this respect with the following results:—

deducting 8.5 cm. from external conjugate, conjugata vera can be accurately estimated. This conclusion is not correct. It may only give an imperfect idea about the conjugata vera. The errors arise from several modifying factors, for example, the amount to be deducted from the external conjugate varies with the thickness of the sacrum and of the symphysis pubis and also greatly upon the elevation of the promontory of the sacrum and length of the spinous process of the last lumbar vertebra. These factors cannot be accurately estimated in the living women and thus the difference between the external and true conjugates varies widely. Skutsch (Stander, 1945) examined 100 pelves and found that this difference varies from 5.5 to 10 cm. In the present series this range lies between 6.25 and 10.75 cm. Of these however, in about 82.5 per cent, the difference lies between 2.5 inches to 3.5 inches and deduction of 3 inches or 7.5 cm. will give an approximate workable idea of the conjugata vera. In the rest, i.e. 17.5 per cent, the difference, as stated before, is above 3.5 inches or 8.75 cm. and deduction of 7.5 cm. will only give an erroneous idea about the conjugata vera. If, however, the external conjugate is found to be 8 inches or 8.4 inches or above, i.e. 20 to 21 cm. or more, conjugata vera will rarely be found

short. Critical measurement for the external conjugate in this series is found to lie between 6.8 inches and 7 inches, i.e. 17 to 17.5 cm. With the external conjugate at or about 17 cm., it is found that conjugata vera is below average in about 45.5 per cent of cases; it is just average in 36.4 per cent of cases and in only 18.1 per cent of cases it is found to be little above the average limit. External conjugate below 17 cm. should be taken as a danger signal and radiological method should be utilized to determine the exact conjugata vera. This is of particular importance in the presence of slightest sign of cephalo-pelvic disparity. In the present series no other external measurement has shown any appreciable relation of any practical importance.

Part IV deals with study of labour.

In this series 43 cases have been studied during labour. Out of these, 40 had vertex presentation and 3 required the help of the forceps. Thus the forceps rate is 7.5 per cent. The forceps cases are analysed below. Average weight of the babies was 5 pounds 8 ounces.

Analysis of the forceps cases

Case 1.—Para 2, 1st still birth, cause unknown. Second—delayed labour, caused by unrotated R.O.P. at the level of ischial spines. Pelvic type—android, conjugata vera—4.2 inches (10.5 cm.), transverse diameter—4.5 inches or 11.25 cm., posterior sagittal—1.8 inches or 4.5 cm., R.W.S.—3.4 inches or 8.5 cm., sacrum—long and flat with deep posterior segment of the pelvis, baby's weight at birth—7 pounds 5 ounces. Cause of delay—lack of rotation and arrest of the head at the midpelvis due to lack of space at this level and bigger head than the average.

Case 2.—Primipara at term, delayed labour due to unrotated R.O.P. at the level of ischial spines. Type of pelvis—gynaecoid, C.V.—3.9 inches or 9.75 cm., transverse diameter—4.9 inches or 12.25 cm., posterior sagittal—1.4 inches or 3.5 cm., R.W.S.—3.3 inches or 8.25 cm., large ischial spines, sacrum—long and flat, posterior segment of the pelvic cavity—deep, sacrosciatic notches—medium size. Lack of rotation of the head is due to lack of midpelvic space. Baby's birth weight—5 pounds 10 ounces.

Case 3.—Para 8, 7 normal deliveries, last delayed labour, due to unrotated R.O.P. at the level of ischial spines. Type of pelvis—gynaecoid, C.V.—3.9 inches or 9.75 cm., transverse diameter—4.5 inches or 12.25 cm., posterior sagittal—1.4 inches or 3.5 cm., R.W.S.—3.7 inches (9.25 cm.), sacrum—small, concavity—good, sacrosciatic notches—wide and gynaecoid, birth weight of the baby—8 pounds 8 ounces. Lack of rotation is presumably due to large head of the baby and consequent cephalo-pelvic disparity at the midpelvic level and also weak uterine contractions.

Comment.—If we take 20 per cent as the average incidence of occipito-posterior presenta-

tion out of all cephalic presentations as stated by Crotty (1935) and Caldwell, Moloy and D'Esopo (1934, 1935), we can presume that out of the 40 cases of vertex presentation reviewed above, 8 cases were occipito-posterior at the onset of labour. Of these latter, only 3 required the help of the forceps and the rest rotated and descended normally without any help. Of the 3 cases where help was necessary, only 1 conformed to the android type and the other 2 belonged to the most favourable of all pelvises, i.e. gynaecoid type. In all these labour was hampered due to relative or absolute narrowing of the midpelvic space. Thus it appears that the size of the pelvis is probably of greater importance than its shape as it is seen that smaller dimensions may cause difficulty in a favourable type of pelvis. On the other hand, if the measurements are good and compensatory space is enough, labour may go on normally even in an unfavourable type of pelvis. Similar evidence has been put forward by Nicholson and Allen (1946). They stated that android type of pelvis *par se* is not associated with difficulty of labour. They are of opinion that obstetric difficulty is significantly associated with lessened pelvic size, particularly with reduced brim-area and with outlet contraction. Thus it is evident that the knowledge of pelvic size and cephalo-pelvic relationship is still of great importance in obstetrics. Pelvic shape while significant in certain respects is only one of many lesser factors that guide the course of labour.

Conclusions

It is only a preliminary communication on roentgenpelvimetric study on the Bengalee and Biharee female pelvis with a view to determining shape and size of the pelvis and its relation to external pelvimetry (clinical) and labour.

Out of the 60 cases studied, 51.7 per cent belongs to gynaecoid type and 25 per cent, 5 per cent, 10 per cent, and 8.3 per cent belong to android, platypelloid, anthropoid and asymmetrical types respectively. Average conjugata vera is found to be equal to 4.16 inches and transverse diameter of the inlet is 4.64 inches. R.W.S. is maximum in gynaecoid and platypelloid types and least in anthropoid. That in android lies between the two. Average R.W.S. is 3.46 inches or 8.65 cm. When it is above 3.5 inches, it is said to be favourable.

External pelvimetry does not give much help in determining the measurements of the pelvic inlet. External conjugate gives only a rough idea about the true conjugate. Deduction from it of 3 inches or 7.5 cm. gives a fair idea about conjugata vera in about 82.5 per cent of cases. In the rest the difference is more than 3.5 inches or 8.5 cm. and deduction of 7.5 cm. will not give the proper idea about conjugata vera. But if the external conjugate is more than 20 or 21 cm., conjugata vera is unlikely to be small. External conjugate of 17 cm. should be regarded as

critical and below this measure should be considered as dangerous and roentgen study should be made to evaluate the true length of the conjugata vera.

Study of labour proved that all the cases that required the help of the forceps had unrotated occipito-posterior presentation due to absolute or relative lack of space particularly at the mid-pelvic level. Pelvic type in these cases was gynæcoid in 66.7 per cent. In other words the size of the pelvis is as important as its shape and perhaps it is a greater factor in determining whether there will be difficulty in labour or not.

The writer is grateful to Mr. L. J. Barraclough and to Dr. G. C. Sen, for their kind and steady encouragement, and to Messrs. Bengal Coal Co., Ltd., for financing this research work. He is also very much indebted to Dr. D. Bhattacharjee, Radiologist, for his sincere co-operation during this study and the trouble he has taken to get satisfactory skiagrams.

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Sarcoptes scabiei. In civil life it is confined mostly in families—poor families especially, and children are the worst sufferers. But in times of war, in the congested camps and in the industrial areas, it spreads like an epidemic and becomes a problem of great national importance.

Due to severe itching especially at night and the consequent loss of sleep there might be definite impairment in the efficiency of the labour or the fighting forces. The loss of man power may at times thus be considerable. In times of emergency, due to lack of proper care and attendance the death rate from its complications, e.g. nephritis, may also be high. Besides it is a very distressing condition and may cause much suffering.

Being a contagious disease it spreads rapidly from man to man by close contact. The start may be at times from animals. The fomites might also be responsible in the spread, specially in dormitories and in cheap living houses.

Various attempts have been made from time to time for a quick and efficient cure of this condition and preventing its spread. The treatment consists in killing the mites and the larvæ and relieving the irritation or the itch. As the mites live inside the burrows under the skin and lay their eggs there, the remedy applied must get at them in the burrows.

The ideal remedy should be an insecticide, quick and effective in its action without being a poison or toxic to the host and non-irritant to the skin. It should be cheap and easily available for mass treatment and its application should be easy which can be entrusted to an ordinary hospital boy or attendant.

From time immemorial sulphur has been the remedy. Sulphur is commonly used in ointment form, rubbed well over the body for 3 or 4 successive nights after a good wash and removal of the scabs. Although it is messy, it is cheap and easily administered. Sulphur has also been used as an emulsion in oil or impregnated in soap where the soap lather is allowed to dry on the body after a body wash.

Treatment with benzyl benzoate emulsion has proved a great advance, but it is not cheap and is not always available. It was first introduced by Kissmeyer in 1937 as an improvement on balsam of Peru. Though it is claimed that both the aqueous and the spirit emulsions act equally on mites (Mallen, 1942) it is doubtful whether the aqueous emulsion is so efficacious. At times it is irritant to the skin and cannot be repeated soon. Oil of turpentine as an emulsion in spirit and soap (Roy and Ghosh, 1944) is another suitable remedy, but it causes burning sensation in the skin.

'Tetmosol', a synthetic drug of the Imperial Chemical Industries, has been claimed to cure

'SCABIES'—REPORT OF 42 CASES TREATED WITH 'TETMOSOL'

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and

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SCABIES or the 'itch' is an infestation of the human or animal skin by the female mites

and control scabies within a short time. It is cheap and easily available. The drug is marketed as a mixture of the following : Tetra-ethylthiuram monosulphide 25 per cent, polyglycerol ricinoleate 10 per cent and industrial methylated spirit 65 per cent. The solution is oily and is of a dark yellowish brown colour. When cold there is a tendency for distinctive yellowish crystals to form which can be readily re-dissolved by gentle heating.

Tetmosol has been used both in liquid form and in soap impregnated with it (Percival, 1942; Clayton, 1943; Bartley, Unsworth and Gordon, 1945; Mellanby, 1945).

We received the 25 per cent solution with instructions to dilute it with water to the required strength immediately before use. If the diluted mixture is kept for some time, the oil may separate leaving out a pasty layer which does not re-dissolve on heating. After diluting with water, the emulsion becomes yellowish white in colour and gives out a distinct odour of hydrogen sulphide; the sulphide gas is probably the sarcoptic factor of the drug. The solution stains clothes yellow but can be easily washed out.

According to Percival (1942) and Clayton (1943) a 5 per cent solution is sufficient to kill the mites. This is made up by mixing 1 part of the 25-per cent drug with 4 parts of water

immediately before use. Three to four ounces of this mixture are required each day for an adult to apply all over the body. When tetmosol is used with soap, it is mixed up with sufficient quantity of soft soap to make up the 5 per cent strength (Bartley, Unsworth and Gordon, 1945; Mellanby, 1945).

The drug was tested by us in two strengths. Twenty-two cases were treated with 12½ per cent emulsion applied once a day for 3 days in the out-patients department and twenty cases were treated with 5 per cent emulsion applied twice daily for 3 days in the in-patients department of the hospital. All cases treated were frank cases of scabies. In all of them presence of mites were looked for, and 19 patients were found to be mite-positive. After the completion of treatment, mites were still present in five out of these nineteen cases. Follow-up was done up to six to eight weeks after the treatment. Patients treated with 5 per cent solution did not suffer from dermatitis but two cases of the 12½ per cent series had it, one mild and the other moderately severe.

Two cases of the 5 per cent series had a second course of treatment after a fortnight's rest.

In all cases the itching and scratching were definitely less after the first day of treatment.

The results are given in table I.

TABLE I

Solution used in the treatment	Number of cases treated	Clinical diagnosis only	Clinical diagnosis with mite found in the lesion	Cured. No relapse	Improved but not cured	No improvement at all	Relapse with fresh crops	Mite negative after treatment	Impetigo	Dermatitis	REMARKS
12½% tetmosol.	22	14	8	5	11	6	7	3	2	2	Tetmosol applied in outdoor patients once daily for 3 days. Total 3 applications.
5% tetmosol.	20	9	11	4	11	5	4	4	4	Nil	Tetmosol applied in hospital cases twice daily (morning and evening) for 3 days. Total 6 applications. Mite + ive in 5 cases after the treatment.

The procedure of treatment was as follows :—

(a) After the diagnosis, the patients received a good bath and were scrubbed with soap and hot water, so that all the burrows were exposed.

(b) The body was dried quickly.

(c) The drug was applied all over the body with a brush from neck downwards and was allowed to dry before the clothes were worn by the patients. (The drug was applied by one of the authors personally.)

(d) The 12½ per cent emulsion was used in the out-patients department; one application was given daily for 3 successive days.

(e) The 5 per cent emulsion was used similarly in the in-patients department twice a day—morning and evening—for 3 successive days. These patients had only one bath before the morning application.

(f) On the 4th day : after a wash the patients were given new clothes. Their bed sheets and pillow cases were also changed.

(g) After the treatment was over the patients were examined every third day during the first week, then once a week from the second week onwards up to six weeks.

(h) Impetigo, if any, was treated with 1 per cent ammoniated mercury ointment when the tetmosol treatment was over.

Summary

(a) Forty-two patients were treated with tetmosol.

(b) Nine patients got cured.

(c) Twenty-two patients improved but did not get cured totally.

(d) Eleven patients had no improvement at all.

(e) Twenty-five per cent cases had relapsed within a week after the treatment.

(f) Two patients treated with 12½ per cent emulsion had dermatitis.

(g) Severe relapse was noticed in 11 cases. These patients did not however come in contact with any scabetic patient during the period of observation.

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ACUTE MYOSITIS

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THOUGH it is a well-recognized fact that striped muscle offers considerable resistance to infection by pyogenic organisms, acute myositis is not uncommonly found, particularly in tropical countries. The term 'tropical myositis' is given to this condition. It occurs in association with lesions in other organs.

Scriba (1885) made a report on four cases of spontaneous muscle suppuration in Japan. Miyake (1904) reviewed 250 cases, all of which had occurred in Japan and added 33 to the list. Ziemann (1913) in the Cameroons made mention of tropical myositis in his official reports. The condition has also been described in French Indo-China by Huard (1933). Cases have also been reported by Tanon and Jamot (1926) in French West Africa, Robertson (1930) in Nigeria, Chesterman (1930) in Congo, McConnell (1923) in Trinidad and by many others in different parts of the tropics.

The following description of the symptomatology of the disease is based upon the published reports. According to Appel (1921) and Traquair (1947) four clinical types can be distinguished, namely :—

Type 1—those with non-suppurating lesions only.

Type 2—those with suppuration lesions but without recurrence.

Type 3—those with recurrent or repeated abscess formation.

Type 4—cases of severe pyæmia with suppurative myositis.

The disease occurs mostly in young adults and adolescents. No age however is immune. There is higher incidence among males than in females.

The onset of the disease might be with localizing signs or without. The disease might start either acutely or very insidiously. In cases starting with local signs, the first symptoms are swelling in the muscles and slight fever. The swelling usually lies under the deep fascia and does not give rise to either œdema or redness. It might affect any muscle. Fever may gradually rise to a maximum of 102° or 103°F. and is usually associated with leucocytosis. As a rule, there is no involvement of the contiguous lymphatic glands.

In cases where there are no local signs at the time of onset, the disease starts very suddenly with high fever going up to 104° or even 105°F. with headache and severe prostration. There is also high leucocytosis, with relative increase of polymorphs. Swellings over the muscles might appear only a week or 10 days later.

In most cases the disease has a tendency to limit itself. Cases with large suppuration will heal up very quickly after incision. Non-suppurating myositis and even small abscesses in the muscle may resolve slowly but completely. In these cases a hard mass remains in the muscle for a very long time.

Most of the early workers attributed the condition to infection by filaria. Later on, conditions like ancylostomiasis, malaria, vitamin deficiency, particularly of vitamin B, sickle-celled anaemia, and debilitated general health have been incriminated. None of these conditions by themselves can possibly explain the inflammation that occurs in muscles in tropical myositis. There is evidence to show that infection is invariably due to a pyogenic organism, mostly *Staphylococcus aureus*. Foci of infection are invariably present, like septic lesions of the feet, either due to trauma or bite of winged pests.

Though Traquair (1947) has said that most of the cases get cured without treatment, penicillin has recently been used with remarkable success.

Case 1.—Indian male, aged 10 years, was admitted to hospital on 10th July, 1945, with a history of continuous fever for 25 days. Patient had a superficial scratch on the foot due to a fall a few days prior to onset of fever. On the 3rd day of fever, he developed painful swellings over the left shoulder, right thigh and right upper arm in front. On examination, the swellings were found to be in the muscles. They were hard and non-fluctuating. Temperature was 102°F. on admission. Total white cell count 26,000; differential count 76 P., 20 L., 3 M. and 1 E. Blood culture positive for *Staphylococcus aureus*. The same organism was grown from serum removed after puncture of one of the swellings. He was put on penicillin, 100,000 units daily. Temperature came down to normal on the 4th day of administration of penicillin and continued to remain normal. The swellings disappeared completely 12 days after admission. He was discharged cured on 25th July, 1945.

Case 2.—Indian male, 32 years, was admitted to hospital on 6th August, 1946, for a large painful swelling over the abdominal wall, just above and to the right side of the umbilicus. Temperature on admission was 100°F. He noticed the swelling 5 days before admission. On examination, the lump was found to be hard, tender, non-fluctuating and situated in the rectus muscle. Culture of the serum drawn from the lump showed *Staphylococcus aureus*. Blood culture was sterile. He was put on penicillin on the 4th day after admission. Penicillin was continued for 5 days. He was discharged cured on 21st August, 1946.

Case 3.—Indian male, age 25, was admitted to hospital on 3rd December, 1948, for swelling over the right side of the abdomen of 5 days'

duration. On admission his temperature was 100 and pulse 90. The swelling was hard, tender, of the size of a hen's egg, situated in the abdominal muscle in the right flank; no oedema or redness. W.B.C. 10,625; differential count 74, L. 18, M. 2 and E. 6. Stools—no ova or cyst. Urine normal. No micro-filaria in the blood. Serum drawn out by syringe from the swelling showed *Staphylococcus aureus* on culture. 100,000 units penicillin were given daily for 7 days. Temperature touched normal on 2nd day after penicillin treatment was commenced. The patient was discharged cured on 13th December, 1948.

Discussion

All the three cases reported above were those of acute non-suppurative myositis. *Staphylococcus aureus* was the causative organism in all. While there was history of superficial scratch on the foot, a few days before the commencement of fever in the first case, no history of trauma or insect bite could be elicited in the remaining two cases. In one of the cases blood culture was positive for *Staphylococcus aureus*. It is not understood why the infection caused by a pyogenic organism should remain non-suppurating and localized to skeletal muscles.

Summary

1. Some of the previous reports on tropical myositis are reviewed.
2. An account of the symptomatology based on these reports is given.
3. Three new cases are reported.

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A CASE OF PARKINSON'S DISEASE TREATED WITH PARPANIT

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WHILE working on certain new antispasmodics Dr. Grunthal (1946) at Professor Kläsi's Clinic, Waldaw, Berne, encountered favourable

results with the preparation G-2747 (of Geigy, Basle). He found that the sensory effects were almost negligible so far as the pressure and pain sensations were concerned. At the same time, muscle sensations and tonus showed highly characteristic changes which were described by a patient as 'Feeling as if the body was of rubber'. The patient felt an uncertainty in the legs. When standing she felt as if she was taller than usual and her joints were made of rubber. The sense of position was also lost and as the patient put it 'It seemed as if I was not myself'.

The workers considering the fact that the sensations in the muscles maintain and control the tonus, studied the effect of the preparation in the diseases which are accompanied by permanent or temporary increase in tonus of the voluntary muscles.

The drug was tried in cases of post-encephalitic Parkinsonism and double athetosis with good results. They considered the drug to be superior to scopolamine and belladonna alkaloids inasmuch as the effects were more intense, lasted longer and the disagreeable effects as dryness of the tongue, difficulty in swallowing, photophobia and giddiness were absent. In fact, this drug had a better rehabilitating effect than any one of its predecessors.

Hartmann (1946) reported the use of this drug in a report of his experience of sixty cases and confirmed the above conclusions. His later contributions of a hundred cases also pointed in the same direction.

Encouraged by the above results the author tried the effect of parpanit in a case of paralysis agitans.

Case record

S. H., aged 40 years, male, was admitted to our care on 19th October, 1948, with the complaint of the shaking of the right side of the body, duration 3 years.

He was a widower and worked as a clerk in a cigarette factory and was not addicted to any drug. Prior to this disease his health had been above average.

Three years back he noticed he had difficulty in writing and holding things with his right hand. Whenever he tried to execute any fine movement with his right hand he used to have tremors. The tremors increased in severity and gradually developed into severe shaking of the whole body and thus incapacitated him for any work. He slept less and though he had a good appetite he could not eat well due to shaking.

On examination the patient was wasted and was very much depressed. He had the typical bent attitude with tremors in the fingers and arms, more marked on the right side. The face was blank and voice monotonous. All the muscles were rigid, the rigidity being more marked on the right side. Cranial nerves were not affected, the sphincters and reflexes were normal and there were no trophic disturbances. The

sensations could not be properly tested as the patient refused to co-operate any further.

Heart, lungs or abdomen did not show any abnormality.

The diagnosis of paralysis agitans or Parkinson's disease was made.

Investigations.—B.P. 110/76 mm. Hg. Weight 7 stones.

(a) Blood: Total R.B.C. 4.2 per c.mm., hæmoglobin 70 per cent (Sahli), total W.B.C. 6,000 per c.mm., poly. 63 per cent, lympho. 28 per cent, eosino. 3 per cent, large mono. 6 per cent, baso. nil.

W.R.—Negative.

Stool examination: Solid well-formed stool, reaction—neutral, no protozoa, no helminth seen.

Urine: No sugar, no albumen.

Treatment.—The patient was given full diet and was put on parpanit therapy according to the following plan:—

Date	Day	Morning	Noon	Evening	
19-10-48	1	1	1	1	(Number indicates number of tablets.)
20-10-48	2	2	1	1	
21-10-48	3	2	2	1	
22-10-48	4	2	2	2	
23-10-48	5	3	2	2	
24-10-48	6	3	3	2	
25-10-48	7	3	3	3	Tremor less, patient smiles at a joke.
26-10-48	8	4	3	3	
27-10-48	9	4	4	4	Parpanit tablets of 0.00625 gm.
28-10-48	10	4	4	4	Parpanit forte tablets of 0.05 gm.
29-10-48	11	4	4	4	Tremor less, patient replies to question.
30-10-48	12	4	4	4	
31-10-48	13	1	4	4	Slight tremor during the evening.
1-11-48	14	1	1	4	
2-11-48	15	1	1	1	
3-11-48	16	1	1	1	
4-11-48	17	1	1	1	

Follow-up notes

6th November, 1948.—Patient had a bad relapse, whole body shaking and mentally very much depressed. Tablets advised in six divided doses.

7th November, 1948.—Tremor less, patient cheerful.

9th November, 1948.—For the first time since the illness patient could write.

10th November, 1948.—Patient discharged with advice to continue the drug and report after a fortnight. Weight on that day—7 stone 6 lb.

25th November, 1948.—Patient cheerful, tremor insignificant but says that the tremors returned whenever he stopped taking the drug.

A specimen of his handwriting on this date is shown on plate XXIII.

Conclusions

The drug had a very good effect on the tremors and the rigidity though the good effects were first noticed as late as the 6th day. But once started the good effect persisted. Another notable feature was the absence of any untoward effect.

On the 19th day the patient had a relapse though that was quickly checked by distributing the drug in six doses instead of three and thereby assuring more constancy in blood level. Whenever the drug was stopped, there was a setback as such the effect of the drug could only be very transitory, hence, for effective therapy the drug will have to be continued—may be throughout the whole life. This drug has a distinct beneficial effect, and as such further clinical trials should be given to assess its real position in the realm of therapy.

Just as one swallow does not make a summer so also one case does not entitle one to an opinion. Yet it must be admitted that the patient was benefited and could return to his vocation which otherwise would have been made impossible by the relentless march of the malady.

I am thankful to Mr. B. N. Chakravarty, Representative, for all the informations required and Messrs. Mallik Brothers, P. O. Kadamkuan, Patna, local distributors of Geigy Pharmaceuticals, who kindly supplied the drug free of cost for clinical trial.

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[For composition of the drug see p. 348.—Editor, I.M.G.]

A Mirror of Hospital Practice

A CASE OF CONGENITAL BILATERAL ANOPHTHALMIA

By R. DWIVEDI, M.B., B.S.

M.O., Shahganj, Jaunpur, U.P.

A FEMALE infant, 4 days old, was brought to me for absence of both her eyes in February 1949.

Family history.—This was the third issue of the parents. Two previous children—1st female, 2nd male—died both at the age of 4 months, 3 years and 1 year previously. They were born healthy and remained so till their death. The parents are both healthy.

On examination.—The child was healthy and well formed. The lids were properly formed and the lower lids on both sides were rolled in, the left more so. There were no eyeballs in the sockets, both being lined with conjunctiva and there was a small blackish, central circular patch in the left socket representing cornea.

There was no other associated abnormality except slight talipes equinovarus in the left foot.

The following description of this condition is given from the 'Pathology and Bacteriology' by Collins and Mayer, 2nd Edition.

'This is a rare abnormality. One or both eyes may be absent. Abnormality met with in healthy and well-formed child. Other associated malformations, hare lip and supernumerary digits. Eyelids, small, but well formed, usually adherent at their margins. Orbit smaller than normal and lined with conjunctiva throughout.

Palpation.—Small nodule—hard, near apex of orbit. Lacrimal puncta may be absent, but lacrimal gland is usually present. Optic nerve never formed to enter the orbit. It either ends as a cone or fibrous filament at optic foramen or it is entirely absent together with optic chiasma.

Cause.—It is a failure of the primary optic vesicle to bud off from anterior cerebral vesicle.

Microscopic examination of nodule.—(a) It is composed of subsidiary parts of the eye, of neuroblastic origin.

(b) No retinal elements.

(c) There is a capsule of fibrous tissue like sclera containing pigmented choroidal tissue.

(d) Complete absence of essential nervous element of eye.

It can be differentiated from microphthalmia, in which nervous element is present'.

I wish to thank Dr. M. A. Alvi, District Medical Officer of Health, Jaunpur, for permission to report this case.

SUCCESSFUL REMOVAL OF AN ELEPHANTIASIS SCROTUM WEIGHING 70 LBS. (35 SRS.) IN A VERY POOR SURGICAL RISK CASE

By N. DAS

Additional Teacher of Clinical Surgery, Campbell Hospital and

M. MUKHERJI

Resident Surgeon, Medical College, Calcutta

S. K. G., aged 62, was admitted to Campbell Hospital in February 1948, for removal of a scrotal tumour.

History.—In 1920, he used to get periodic attacks of funiculitis and epididymo-orchitis on both sides. The scrotum started swelling from then and in 1940 it was about the size of no. 4 football. As he had a high blood pressure (175/100) and enlarged heart, surgeons were not agreeable to do any operation on him. The scrotum went on increasing in size with periodic attacks of filariasis till at last it reached his ankle (figure 1, plate XXIII). His blood pressure remained persistently high and the heart got more enlarged. Moreover, he had some cardiac attacks recently.

Examination findings.—General health satisfactory. Haemoglobin 70 per cent. Neck veins prominent. Heart enlarged. Apex in 6th left

intercostal space in anterior axillary line. B.P. —180/100.

Bleeding and coagulation time, 3 and 2½ minutes respectively. Blood urea—30 mg. per 100 cc. Serum protein—6.2 gm. per 100 cc. Urine—nothing abnormal.

In view of the cardiovascular disorder, physicians were consulted as regards the safety of operation. But they gave a very guarded opinion, and operation could not be decided upon. After 15 days' rest in hospital the patient's cardiac condition improved and he became very much anxious for the operation. With the concurrence of some physicians an operative removal under local anæsthetic and a basal narcosis was decided upon.

Operation.—Pre-operative medication—morphia ¼ gr. Anæsthesia—local novutox ½ per cent 300 cc.

Penis was dissected out first by a vertical incision from symphysis pubis. Then a circular incision was started on both sides of the neck of the scrotum from the vertical cut. The testes with hydrocele sacs were delivered out and the hydrocele sacs were excised. The circular incision across the neck of scrotum was then completed by extending the two lateral incisions to meet behind the scrotum. The tumour was then removed after ligaturing all vessels. It required two men to remove the scrotum from the table. The operation took 45 minutes.

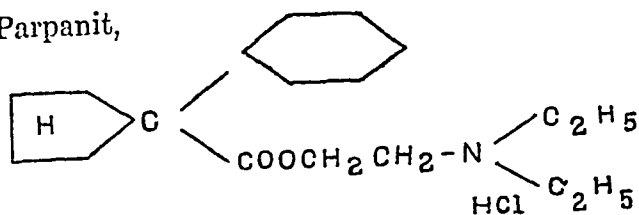
During the early phase of the operation the B.P. rose to 200/100, but it fell to 100/60, just when the tumour was detached from the body. 500 cc. of plasma was administered intravenously and the B.P. rose to 140/80 in 20 minutes' time. 300 cc. of blood was transfused slowly after this and the patient recovered from the shock.

The patient had an uneventful recovery except that the preputial skin of the penis sloughed out, necessitating a Thiersch's graft. Figure 2, plate XXIII, shows his appearance after the operation, the gauze dressing indicating the site from which the graft was taken.

Occasional Notes

THE DIETHYLAMINOETHYLESTER OF PHENYLCYCLOPENTANE CARBOXYLIC ACID (PARPANIT) GEIGY IN THE TREATMENT OF DISEASES OF THE EXTRAPYRAMIDAL MOTOR SYSTEM

Parpanit,



was synthesized in 1945-46 in the laboratories

of J. R. Geigy, in Basle, and pharmacologically tested by Domenjoz (1946).

The first clinical tests were made at the outpatients department for nervous diseases, University of Zurich, by Hartmann (1946, 1947), and at the Psychiatric Clinic, Waldau, by Grunthal (1946). Parpanit, belonging to the group of spasmolytics, evidently shows best results in the treatment of basal ganglia disease and extrapyramidal disturbances with hyperkinesis. Best results have been obtained in rigor of post-encephalitic origin, in intentional tremor, in paralysis agitans, double athetosis and in a single case of Little's and Wilson's disease. Tremor is not so easily influenced by parpanit although it may be decreased.

The mode of action of parpanit is still not quite clear. Electromyograph and electroencephalograph findings make it likely that the new drug acts like a filter by suppressing the incoming involuntary stimuli of the muscle fibres to some extent before they reach the central nervous system.

The doses vary from 25 to 75 mg. given several times daily orally. The drug is non-toxic even when given in considerably higher doses. The first sign of overdosing is slight transitory dizziness. Parpanit is excreted within 2 to 3 hours and it is therefore advisable to spread out the daily medication in 4 to 5 or even more single doses. Addiction or tolerance has never been seen not even after prolonged application of one to two years' duration.

The main advantage of parpanit over the older medicaments is the lack of untoward effects on the vegetative nervous system. There is no diminution of salivation, and accommodation is not affected.

It is not easy to institute parpanit treatment, especially not when switching over from alkaloid treatment to parpanit. The withdrawal of the alkaloid should not be made rapidly. It is better that both medicaments, i.e. the old alkaloid and the new parpanit, should be given simultaneously, gradually diminishing the alkaloid and slowly increasing the parpanit medication, while all the time the patient is kept under medical control. Generally, this change-over process should last from two to three weeks. The initial dizziness at the beginning of the parpanit medication, which is quite often disturbing in elderly patients, is generally overcome by administering the next smaller tolerated dose for several days. Later, higher doses can be administered. In arteriosclerotic Parkinsonism, especially of old age, this dizziness may be quite severe and may not allow parpanit medication at all. It therefore needs plenty of patience and endurance both from the patient as well as the doctor to find out the optimum dose for each individual case. Generally, over 60 per cent of the treated patients show an

improvement of the previous state amounting to about 25 per cent.

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Therapeutic Notes

DEHYDRATION AND ITS TREATMENT

Part II

By R. N. CHAUDHURI, M.B., M.R.C.P., T.D.D.

Professor of Tropical Medicine, School of Tropical Medicine, Calcutta

Salt Deficiency

THIS occurs when water and salt are lost while the patient is taking water freely or being given parenteral glucose but no salt. Such losses commonly come from digestive juices which contain a large volume of water and have predominant sodium and chloride ions (total daily secretions approximate 2 gallons with 2 oz. of chlorides) and hence are seen in diarrhoea or vomiting. The latter is usually of a protracted form as in pyloric stenosis or toxæmia of pregnancy in which water intake goes on while sodium and chloride are being continually drained, so that effects of salt deficiency tend to dominate the picture. Other digestive causes are prolonged gastric or intestinal suction and intestinal fistula. Salt deficiency may also occur through excessive sweating, accompanied by free drinking of unsalted water. Familiar examples are seen in firemen and stokers. Sweat itself is a hypotonic fluid, still quite an appreciable amount of sodium chloride may be excreted when sweating is profuse. But salt deficiency is not necessarily an acute or sub-acute condition, for smaller losses prolonged over days or weeks can also cause severe depletion, particularly if salt intake is lowered.

In this deficiency the burden falls on the extracellular fluid which becomes hypotonic from abnormal loss of salts. As this is liable to upset the osmotic equilibrium, the kidneys try to remedy it by excreting water. This causes dehydration, because the excretion of water may amount to a large volume; a 70 kg. man depleted of 1 oz. of his body salt, for example, needs $3\frac{1}{2}$ litres (6 pints) of isotonic saline to restore the normal balance. Owing to the renal activity, the urine volume is not decreased at first and may indeed be increased; it is more dilute and

chloride is absent except in Addison's disease. As there is no cellular dehydration, thirst is absent; indeed water is often repellent as it tastes insipid. Cramps develop when depletion of salt continues. The patient suffers from lassitude, weakness, headache and tendency to fainting on standing up. Appetite becomes poor and there may be nausea and vomiting, thus starting a vicious circle. The plasma sodium and chloride fall. Rise of blood urea, mental apathy and general exhaustion are greater than in water deficiency. There may be marked mental changes, e.g. confusion and delusion. In severe cases water by mouth is very slowly excreted, which, as Marriott (1947) suggests, may be due to atony of the stomach and delayed absorption, a condition which may lead to the wrong diagnosis of acute dilatation of stomach. Usually there is some disturbance of acid-base equilibrium caused by disproportionate loss of sodium and chloride ions from the digestive secretions. Vomiting causes a relatively greater depletion of chlorides and tendency to alkalosis. Diarrhoea, on the other hand, has the reverse effect with disproportionate loss of sodium and a tendency to acidosis.

With the progressive loss of fluid, the plasma volume is reduced, but tends to maintain itself at the expense of the tissue fluid, and when this source fails, circulatory disturbance becomes manifest. A systolic blood pressure below 90 mm. Hg. probably indicates at least a 25 per cent reduction of plasma volume, but in some cases as much as two-thirds of it may be lost (normal plasma volume is about 3 litres). As a rough rule, plasma loss multiplied by 6 gives the total extracellular fluid loss (Marriott). Reduction of plasma volume is accompanied by hæmo-concentration, increased viscosity of blood and diminished urine, and the patient passes into a state of circulatory collapse or shock. He is pallid with sunken eyes, cold extremities and collapsed veins. Anuria occurs when the blood pressure falls to about 70 to 80 mm. Hg. and finally there is stupor and coma. Unless the true nature of the condition is recognized, deaths are ascribed to uræmia, toxæmia or circulatory failure.

A form of chronic salt deficiency must be mentioned which is more common among unacclimatized Europeans in the hot weather of the tropics who excrete increased amount of sodium chloride in their sweat. Its effects are more insidious; lassitude, apathy, undue fatigue and poor appetite. Such persons are benefited by taking extra salt.

Mixed water and salt deficiency

This occurs from abnormal losses of secretions, but the patient is not taking water freely. It is common in any condition with acute vomiting. Most patients have a mixture of the symptoms of pure water and of pure salt depletion. The extracellular fluid volume is

reduced and tends to be hypertonic owing to the disproportionate water loss, and this tendency causes some withdrawal of water from the cells. The clinical picture is that of salt deficiency as described above; patients are also thirsty and have dry mouth and early oliguria.

Thus we see that the body may become fluid-deficit from lack of water, salt or both. In the first case the loss is distributed over the whole volume of body water, including the intracellular fluid; this accounts for the great thirst. In salt deficiency, only the extracellular fluid is affected, the blood volume is early reduced and hence the great weakness. 'For any given amount of fluid loss, the effect on plasma volume and so on circulatory efficiency will be about three times as great when the fluid loss is due to salt as when it is due to water deficiency (Black). In ordinary practice clear-cut deficiencies as described above are not common and patients often show a fluid imbalance somewhere between water and salt deficiency, its degree depending on the nature and amount of fluid lost and on the food and water taken by the patient. The most frequent causes are diarrhoea and vomiting.

Fluids used in dehydration

1. Water.
2. Sodium chloride solution—
 - (a) Isotonic (normal)—0.85 per cent or lesser strength.
 - (b) Hypertonic—1.1 per cent.
3. Glucose solution—5 per cent.
4. Plasma.

Water.—This is indispensable in dehydration. Fluid by mouth is easily absorbed, more satisfactory and better retained than any fluid given parenterally. Moreover, there is no risk of overloading the circulation. In severe salt deficiency, however, when the patient is collapsed, water given by mouth tends to collect and overfill the stomach from which it may be regurgitated or vomited with risk of being aspirated and infecting the lungs, owing to depression of the cough reflex. It is also dangerous to give much water either orally or intravenously when the blood pressure is low and anuria develops. For then the water, being unable to pass out, enters the cells and may cause symptoms of water intoxication—vomiting, epigastric distress, disorientation and convulsions leading on to coma and death.

Sodium chloride solution.—This is most valuable in dehydration secondary to salt deficiency, as it supplies at one and the same time the water and the lost electrolytes. Saline is also of help in correcting states of acidosis and alkalosis. Though it is usually given parenterally, half normal saline or an equal mixture of normal saline and glucose solution is often tolerated orally. A normal saline contains 9 gm. of salt per litre, while most body fluids contain 6 gm.

per litre; the excess is excreted by the kidney. But even in health, the power of the kidney to excrete salt has definite limits (not more than 2 per cent in urine) and the use of excessive amounts adds to the work of the kidneys and may lead to its retention and oedema of the body. So as soon as the symptoms are relieved, isotonic saline should be discontinued in favour of 5 per cent glucose or hypotonic saline, if intravenous infusion needs still to be continued. Infants have far less power than adults of excreting salt. Normal saline is a dangerous drug to them and suitable concentrations are $\frac{1}{4}$ or $\frac{1}{5}$ isotonic, which is prepared by mixing one part of normal saline with three or four parts of 5 per cent glucose. Hypertonic saline is used only in severe forms of salt deficiency, such as cholera, when several litres of saline fluid are lost in a few hours.

Glucose solution (5 per cent).—It serves the following purposes: (1) It is a good vehicle for supplying water when this is to be given parenterally. (2) It supplies some calories, since often the patient is starving. (3) It promotes the oxidation of any ketones that may be present. (4) It promotes diuresis (probably in stronger solutions). Glucose is given for water deficiency and has in itself no value in salt deficiency unless combined with salt.

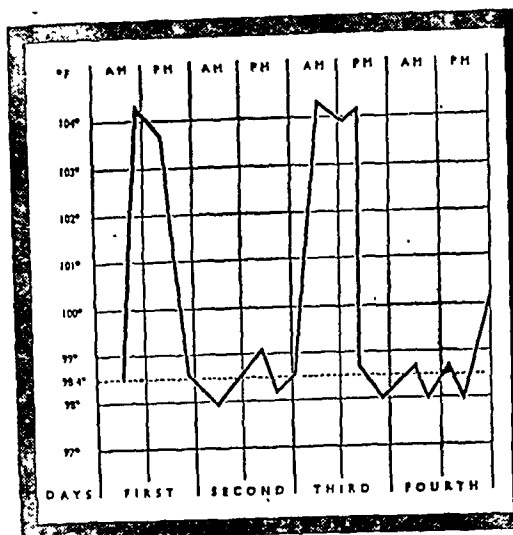
Plasma.—It is used in circulatory collapse in which saline and glucose are only of temporary benefit because they rapidly leave the blood vessels. Plasma increases the lowered volume of circulating blood and raises the intravascular osmotic pressure owing to its protein and salt content, the latter being approximately the same as in normal saline.

Routes of administration

In relatively minor degrees of dehydration or as a prophylactic measure, the oral route is sufficient. If the patient has difficulty in drinking or is comatose, a valuable method is continuous drip method through a Ryle's tube passed *via* the nose into the stomach. Another way is through the rectum. Intravenous route is the method of choice when the fluid must be given as speedily as possible or when gastro-intestinal irritation is present. To prevent reactions, the solution should be free from pyrogenic substances. Subcutaneous injection may be used, but in many instances the circulation is so defective that there may be considerable delay in absorption of the fluid. In infants and young children, the intraperitoneal administration of fluid may be satisfactory at times. Glucose (except perhaps in 5 per cent solution) is inadvisable for subcutaneous or intraperitoneal injection as it may be irritating to the tissues. There is also the risk of collapse in cases of severe salt depletion, because the sodium and chloride ions from the already depleted plasma rapidly diffuse into the tissue depot of injected glucose solution.

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Indian Medical Gazette

AUGUST

ACUTE ANTERIOR POLIOMYELITIS

LIKE most other crippling organic diseases of the nervous system this disease does not thrive in India (Grevil, 1946). Its occurrence, however, is not unknown. While subjects crippled by it are comparatively rare, atrophy of small groups of muscles in an otherwise well-built subject, like an army recruit, is often seen.

Cases of the disease have this year been reported from Bombay and Delhi, and we understand that 12 cases have occurred in Calcutta up to date, 24th September, 1949, reported in this delayed issue for August 1949, also. At the present moment there exists in the whole country a scare of the disease. Iron lungs have been received from America (Medical News, 1949). An attempt has been made in the lay press by a well-known medical man to allay the scare (Chand, 1949). An article for further allayment appears elsewhere in this issue (Viswanathan, 1949).

The New Zealand epidemic.—An admirable account of the disease, as it has occurred in an epidemic form in New Zealand, has become available recently (Caughey, 1949). The following items are selected for special attention :

(1) *The epidemic type of the disease.*—It is characterized by (i) influenza-like symptoms, (ii) high mortality, (iii) muscular spasm, and (iv) hyperæsthesia of the skin.

(2) *Change in the age incidence.*—There is an increase in the incidence in the age group over 16 and decrease in the age group 0 to 5.

(3) *Contact cases and multiple cases in one house.*—These cases show that the infectivity of the virus has increased.

(4) *Severity of the disease in relation to the onset of the epidemic.*—Earlier cases are more severe.

(5) *Portal of entry.*—Children are more susceptible immediately after tonsillectomy. Operation on nose, throat and teeth are contraindicated during an epidemic.

(6) *Three stages of the disease.*—They constitute (i) stage of invasion (or minor illness) which may be referable to as the cold of the upper respiratory tract or of the gastro-intestinal tract, and lasts 2 to 3 days, settling down without any ill effects (hence the name 'Abortive Poliomyelitis'); (ii) stage of pre-paralytic poliomyelitis in which, in addition to the usual aches and pains, stiffness of the muscles of the limbs

and back develops, without any paresis; and (iii) stage of paralytic poliomyelitis in which paresis is present.

(7) *The CSF may show changes in the second stage.*—Pressure is usually moderately high. Cell count varies enormously, 5 to 2,000, preponderance of polymorphs changing later to one of lymphocytes. The count becomes normal in 2 to 3 weeks. Protein content is normal or only slightly raised but rises as the cell count falls. Glucose and chloride are unchanged. The changes give no indication of the serious development of paralysis.

(8) *Treatment.*—It consists of (i) providing a firm flat mattress and a low pillow, (ii) sand bags and a cradle, if necessitated by pains in the legs, (iii) hot packs for the spasm of the muscles, (iv) passive movements within a day or two of beginning the treatment, (v) re-education of the affected muscle a few days later, (vi) ambulation as soon as possible, and (vii) the use of a respirator, if necessary. The respirator is taken in use as soon as it is indicated. The only danger in this treatment is from aspiration of food, vomit, etc. All food by mouth is stopped and a tracheotomy is performed. The feeding is done by the intravenous route (glucose, saline, protein hydrolysate or plasma—1 bottle daily). Prophylactic penicillin is given. A patient may require these measures for a week or two.

(9) *Result of treatment.*—Of 224 patients, 12 died, 32 still had residual weakness after 12 months and the rest recovered completely.

The Nicobar epidemic of 1947.—An account of it was given in this journal last year (Moses, 1948). The epidemic appears to be of considerable interest in studying the wave of epidemiology in the East. The infection was traced to the Andaman Islands. Incidentally, the writer of the account drew attention to four special characteristics of the population of the Nicobar Islands :

(1) *Isolation.*—The people are living by themselves without any intercourse with India. Once in 3 months a steamer from Madras arrives close to the islands and lands goods and stock for the officials from Madras. Very occasionally a daring trader goes to the Andamans. One such trader was supposed to have brought with him the disease.

(2) *Special plan of houses.*—They are hollow spheres resting on raised platforms. The entrance is through the floor (from under the platform). There are no windows. Overcrowding in such dwellings is a genius of the people.

(3) *Adenoids.*—Due to overcrowding and lack of ventilation adenoids are almost a normal anatomical feature and responsible for a characteristic facial expression.

(4) *Water not used as a drink.*—Milk from green coconut is the universal beverage. Water is used for washing and cooking only.

Other recent work of clinical interest.—From a summary of previous studies emerge the following: (1) Cases needing the respirator do not do well on the whole, even after an immediate recovery and discharge from the apparatus. (2) Oxygen should be used in addition to the respirator as indicated by Millikan's oximeter. (3) Rectal or subcutaneous feeding is to be preferred to intravenous feeding in view of the œdema of the lungs which is feared. (4) Bulbar involvement is the dreaded complication: involvement of the nucleus ambiguus is indicated by dysphagia and alteration in the voice while that of the reticular formation of the lower medulla by the alteration in the respiratory rhythm, flushing and fall in blood pressure (Rivers, 1948).

Negative signs.—They have also been stressed recently and consist of: (1) cough other than that of laryngeal involvement, (2) diarrhoea, (3) mental clouding, (4) convulsion, (5) rigor, (6) rash, (7) palpable spleen, (8) stiff limb, as opposed to weak, floppy or flabby limb, and (9) persistence of fever after 12 days (Powel, 1949). All of them have been made dogmatic intentionally, some are more so than others.

Recently cases diagnosed as non-paralytic poliomyelitis have been found to be suffering from mumps meningo-encephalitis, showing the unreliability of clinical diagnoses (Kilham, Levens and Enders, 1949).

The Kenny treatment.—It has been commented upon in the House of Commons (National Health Service, questions to the Minister, 1949). It has been included in the selected items in paragraph 3. Details as to the care of individual muscles may be obtained from a brochure on the Kenny method of treatment from the National Foundation for Infantile Paralysis, U.S.A. (Hyman, 1946).

Chemotherapy.—'A number of polio victims were said to be walking around to-day, thanks to the chemical called phenosulphazole, with trade name Darvisul, instead of being paralysed and crippled for life' (Medicine, 1948). This good news has not been confirmed.

Prognosis.—The electric reaction of the affected muscles is indicative of recovery (Mackenzie, 1949; abstract in Current Topics in this issue, p. 372).

The virus, etc.—From studies on the virus in recent years has emerged a composite group, the Lansing type (from Lansing, Michigan, U.S.A.). It consists of 4 strains including YSK and MEF. Immunologically, they are interrelated. The natural antibody titre of the human serum, against the type, increases with age. Ultra-

violet-inactivated Lansing virus and formalin-inactivated Lansing virus are capable of immunizing mice and cotton rats. Active virus can immunize monkeys. Application of these processes to human beings has not so far been made (Rivers, *loc. cit.*). Probably they will provide the only sure prophylaxis. Convalescent sera and anti-viral sera prepared in the horse are useless (Parish, 1948).

Points in epidemiology.—Lately communication between India and the Andamans has increased. Displaced persons, refugees and business men have gone to prospect. Many have returned. Most of them went from West Bengal and returned to or through West Bengal. The bearing of this movement on the reported incidence of poliomyelitis in India is not yet known.

In England the disease is again approaching the incidence of 1947 which was rather heavy. From this increased and widespread incidence, including geographical tracts previously entirely free, it appears that a pandemic of poliomyelitis is in the making.

Prophylaxis, etc.—One single measure which can be usefully directed against the disease is prevention of overcrowding such as occurs in cinemas, swimming pools, community bathing in holy waters and congregational worship under one roof. Fatigue and chills must also be avoided. But unfortunately it must be added that prophylactic measures have failed singularly in checking the disease (Editorial, 1949b). On the other hand it has been feared that a high standard of living and superior sanitation make the community concerned more liable (Horstmann, 1948). The fear caused by this observation has been allayed recently (Hill and Martin, 1949). A very significant observation against infection by droplets has been made: the disease in England shows a high incidence in autumn when other infections caused by droplets show a low incidence (Editorial, 1949a). Exclusion of flies, water and milk does not appear to make any difference whatsoever.

To add to the thorns of a thorny problem of poliomyelitis the hedgehog has crept in unexpectedly. Two animals were found in unusual places in England. One of them was paralysed. The other which was not paralysed has left behind dried spoor which is awaiting investigation (Wilson, 1949; Spicer, 1949). Moles have been suspected for some time as natural reservoirs of the disease. They, cotton rats and Swiss mice have been infected experimentally (Rector, 1949; abstract on p. 370).

Emboldened by the defeat of the epidemiologist a non-medical observer in England has suspected peaches for the following reasons: (1) During the War when peaches were not available there was little evidence of infantile paralysis. (2) After the War when peaches were placed on the market the incidence of the

disease rose. (3) Peach skin is furry and porous, unlike that of an apple, which is hard and smooth and can be cleaned better. (4) In Canada, incidence is said to increase every year when peaches are ripe (Maddison, 1949). The peaches, fresh and tinned, may be avoided as well. Peach jam may be safe.

Adverse tellural influence on the virus in India.—The fact that improvement occurs in the paralysis up to a year has been considered to be an evidence of the chronic nature of the infection. If the polio scare is found to be correct (by an increased incidence of the disease) and the damage negligible (as is usual, so far), the correctness of the adverse tellural influence on the virus in India will have been proved. That will suggest the utility of tellural hospitals in India for the treatment of cases of polio contracted in Europe and America (Greval, *loc. cit.*).

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Special Article

POLIO

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Why talk about polio ?

THE word 'polio' has been striking the headlines during the recent weeks in Indian newspapers. A certain amount of scare has therefore been produced in the mind of the public. It is no doubt true that a fairly large number of cases of polio have been reported in Bombay city. A few isolated cases have also been reported from other parts of India like Delhi and Calcutta. It has not yet been decided whether the cases that have been reported in Bombay constitute an epidemic in any form or they are only an evidence of better recognition of the disease, due to an awareness of the condition in the minds of medical men. That the disease has been in existence in India for a long period of years, is shown by the fact that many cases of paralysis due to previous attack with polio have been seen in the Orthopaedic Departments of general hospitals. The possibility of its assuming epidemic proportions in any part of India cannot be gainsaid. It was only in 1947 that there was a very serious epidemic of polio in Car-Nicobar Islands of the Andaman group. Nearly 10 per cent of the population were affected by the disease. There was mortality rate of 17.7 per cent among the afflicted. The importance of polio as a public health problem lies not so much in the mortality associated with the disease as it is in its crippling after-effects amongst those who survive the infection. It is, therefore, essential that we should talk about this condition in order that not only the medical men but also the general public should have a clear idea as to its nature, to enable them to recognize it in its early stages.

What is polio ?

Polio is the abbreviation for acute anterior poliomyelitis. It is a disease of the nervous system caused by infection with a virus. The disease is characterized by fever which lasts 4 to 6 days, headache, pain in the back of the neck, sometimes painful spasm of muscles and subsequent paralysis.

How is polio caused ?

Polio is an age-old disease, but it was only clearly recognized as a clinical entity in the first half of the last century. Small outbreaks were recorded in St. Helena in 1834, in England in 1834 and in the United States in 1843. The

first large epidemic occurred in Scandinavia in 1868. More recently extensive epidemics have occurred in Australia and New Zealand. It is of considerable significance that the countries most severely affected have the highest standard of living and of hygiene and sanitation. As other countries have attained comparable standard, they in turn have suffered extensive epidemics. This is probably due to increased susceptibility of a protected population to a new strain of the virus when it is imported accidentally into that community.

Recent researches have shown that the disease is due to infection by a virus. Several strains of the virus have now been determined some pathogenic to mice and others to monkeys and men only. If one suffers from the disease and recovers from it, one develops immunity to subsequent infection by the same virus. As, however, there are many strains of the virus, a second attack of the same person by a different virus is possible.

Prior to the recent war polio was thought to be a rare disease in the tropics. It is, however, now clear from the observations made during the recent war that the disease is a common infection in the tropics.

In the South African epidemics of 1944 to 1945 it was noted that the Bantu were less liable to paralytic poliomyelitis than Europeans. It has also been reported that a large number of cases occurred in India during the war amongst British soldiers, while very few occurred amongst the Indian soldiers. It has been suggested that there may be inherent physiological differences in the susceptibility of the two races. Diet has also been incriminated to account for this difference. It is known that diet influences the susceptibility of experimental animals to polio. Thus mice fed on a diet deficient in thiamin are less susceptible to infection with the polio virus than are normal mice. It may well be that the inadequate staple maize diet of the African natives accounts for his relative resistance to polio. Another explanation that might be given is that the African native in his insanitary surroundings living in primitive conditions is regularly exposed to infection with endemic strains of the virus of polio and so acquires an immunity not shared to the same degree by the more hygienic European.

In the temperate zone, polio is essentially a disease of the warm weather months. It occurs usually in the month of August and September in the Northern Hemisphere and in the months of March and April in the Southern.

The methods of spread of the infection in a community have been extensively studied by various workers. It was originally thought that droplet infection by healthy carrier was the usual mode of transmission. During the war it was seen that the incidence increased with that of bowel diseases. It has been shown during

recent epidemics that the virus content of sewage in an epidemic area is very high, showing that contamination might be the mode of spread. It has also been recently found that the virus is limited more to the post-nasal area and as such its spread by droplet infection could not be so easy. Animal experiments have also shown that injected virus was excreted in the faeces and could be recovered from it. The virus has occasionally been isolated from the throats and has repeatedly been isolated from the faeces of apparently healthy contacts of cases. It can be regularly isolated from the group in intimate association with the patient such as the family contacts. This group may remain infected for as long as 2 months after the occurrence of the first and may be the only paralytic case. The high incidence of infection among household contacts has been emphasized by a number of investigators, in contrast to the relatively lower incidence among extra household contacts and the still lower incidence among non-contacts in the same neighbourhood. This indicates that there has been no widespread infection in the neighbourhood caused by the same factor in the environment common to all. It is, therefore, suggestive of an infection existing in the household. The infection takes place by contact. Infection of contacts may take place from virus in the secretion of the throat and from virus excreted in the faeces. The last word has, however, not been said about epidemiology of polio. There is general agreement based on available evidence that the spread is from human to human. It is not clear whether the spread takes place *via* respiratory droplets or *via* hand-to-mouth contamination. From the public health point of view perhaps, it is not important as long as it is recognized that infection takes place from human to human. It seems probable that polio may be spread both as a droplet infection and as an alimentary infective disease. If the latter is also accepted as one of the modes of spread, the possibility of an intermediate factor like the house-fly which might carry contaminant to ingested food material, should also be borne in mind. During epidemics inactivity of the fly in the affected locality has been shown to be very high.

Pathogenesis of polio

In whatever way polio is spread, there is no doubt that of those infected only a minority develop symptoms and still fewer develop paralysis. Laboratory studies suggest that for every 10 persons infected only one will have symptoms. The question as to why the unlucky few develop paralysis is obviously an important one. It has long been suspected that undue fatigue and violent exercise predispose a person to a paralytic attack. It was recently shown by Russell that all the severely paralysed cases in his series had undergone severe exertion within a probably significant period before the onset of illness. The rôle of tonsillectomy is still in

dispute. As, however, infection of tonsils is very liable to produce a bulbar form of the disease, it is advisable not to submit children to tonsillectomy during an epidemic of polio. The mode of invasion of the nervous system by the virus is of considerable practical and theoretical interest. It has now been proved that it does not enter through olfactory nerves. In fatal human cases the virus has been found not only in the nervous system but also in the pharyngeal mucosa, in the jejunal wall and in the faecal contents but not in the wall of the large intestine. It is generally agreed that the virus gains entrance to the nervous system *via* the axons of nerves. The nerves supplying the throat are specially implicated. Recent studies of Field and Brierley show that the virus might enter the nervous system by lymphatics. In the body, as in the community, there may be several routes by which the virus spreads.

In the nervous system the virus usually affects the anterior horn-cells of the spinal cord and brain stem and the thalamus and the motor area of the brain.

How to recognize polio ?

The diagnosis of poliomyelitis must be based primarily on symptoms and clinical findings. The earlier in the disease a case is seen, the less characteristic these are. In addition, certain laboratory observations are of value, but none which is available to the clinician is absolutely diagnostic. For recognizing a case of polio the history of onset and course must be compatible with polio, that is, acute onset of a febrile illness, sometimes resembling influenza with headache, fever and a recognizable stiff neck as determined at least by some disinclination to forward flexion of the head. Vomiting may or may not be present. The fever rarely exceeds 104°F. and does not last longer than six days, unless obvious secondary complications of bulbar palsies develop. Six to 12 days are given as the incubation period for the disease. During the initial febrile period no paralysis is seen. Gastro-intestinal upset like diarrhoea is often noticed during this stage. Irritability, restlessness, depression, and inversion of the sleep rhythm are also noticed. Stiffness of the back of the neck, back-ache, particularly in the lumbar region, shooting pain along the nerve roots or in groups of muscles and muscle spasms are often noticed before actual paralysis sets in. In 3 to 6 days after the onset of fever paralysis of muscles occurs usually attaining its maximum in a few hours, sometimes all the 4 limbs may be paralysed within a short time and remains in that state for a few days. The extent of paralysis diminishes rapidly in a few weeks. With the appearance of paralysis the fever gradually comes down. If any group of muscles continue to remain paralysed after this period, recovery from paralysis will take a long time, often the paralysed group of muscles remain

paralysed permanently, producing thereby the various crippling after-effects of this disease.

For purposes of recognition of the disease the course can be divided into 3 stages, i.e. the pre-paralytic stage, paralytic stage and the post-paralytic stage. The difficulty in recognizing the disease in pre-paralytic stage has already been indicated. Diagnosis in the paralytic stage is easy depending upon the part of the nervous system that is affected. Three forms of the disease are described, the spinal cord form, brain stem form and encephalitic form. It used to be considered that the third form, which affects the cerebral cortex, was not really due to polio virus and the cases with cerebral manifestations were considered to be due to infection by other types of virus like measles, chicken-pox, smallpox, etc. The 1947 epidemic in England has however shown that the cerebral forms of polio do occur during an epidemic. In the spinal form when it occurs in young children, the paralysis is often not apparent until the second or third day of the illness. In older children and in adults, the paralysis is usually present within 24 hours of the onset. The paralysis is always of the flaccid variety with loss of the deep reflexes in the region of the paralysis and subsequent atrophy of the muscles, if it is lasting. In some cases the paralysis spreads rapidly from its original site, either in ascending or more rarely in descending fashion. The ascending cases are very liable to be terminated with fatal bulbar involvement, and invariably produce respiratory paralysis. A case of this type was reported from one of the hospitals in Delhi in a young adult. The paralysis is generally much more widely spread at the onset than it is destined to be permanently. At first all four limbs may be completely helpless and later there may be complete recovery in all but one limb. The widely spread temporary paralysis is due to a recoverable affection of the nerve cells, whereas the permanent palsy is the result of an actual destruction of the cells. Disturbances of objective sensation are rare and are invariably transient. There might be slight impairment of pain and temperature sensibility. Subjective disturbances on the other hand are common and consist of severe local pains in the limbs, back and neck. Muscles may be very tender to the touch. Pain on moving the joints may be felt and may persist for weeks. Respiratory paralysis may occur in the spinal form either as a result of paralysis of intercostal muscles or paralysis of the diaphragm or both. When the intercostal muscles alone are paralysed, there may be no respiratory distress but inspection will show that the breathing is weakened and is mainly diaphragmatic. When the diaphragm is paralysed as a result of lesion affecting phrenic nerve centres, breathing will be wholly thoracic. Only when both intercostal muscles and diaphragm are paralysed, will there be respiratory failure.

In the bulbar type, the pre-paralytic period may be 24 or 48 hours. The first indication of paralysis is usually reflected in some difficulty in swallowing fluid. The parents frequently volunteer the information that the child's voice has a nasal tone. As the condition progresses, inability to swallow becomes more severe and mucus and saliva collect in the back of the throat. There are usually associated palsies of the muscles supplied by cranial nerves. Facial paralysis is quite common. There may be paralysis of the tongue muscle. Double vision is a frequent complaint and paralysis of one or more of the eye muscles may occur.

Encephalitic form.—This form might occur alone or be more commonly associated with the bulbar form. The prodromal symptoms are frequently of very short duration and may even be absent. The state of meningeal irritation is accompanied by a higher temperature, usually 104° to 105°F., a greater degree of prostration, extreme irritability and at times somnolence or even stupor. This type is only occasionally associated with the paralysis of spinal nerves and muscles. The prognosis in this type is very poor.

When there is polio scare in a place, the layman will naturally ask the doctor, 'What symptoms should I look for?' The reply should be something like the following:

'If your child is ill with fever, sore throat, a stomach or bowel upset, restlessness, apprehension, the diagnosis may be any one of many minor illnesses; but if in addition your child complains of headache, has a tremor, stiff neck, rigid back, tender muscles, enlarged tender cervical lymph nodes and wants to be left strictly alone, call your doctor immediately, because the chances are 5 to 1 that your child has polio'. At this stage the diagnosis can be made more conclusive by a lumbar puncture. The most constant finding is an increase in the cell count, which may be as high as 2,000 per c.mm. The cells are most commonly lymphocytes and mononuclears but polymorphonuclears have been found to be present in half the total number of cases in some epidemics. The protein content of the cerebro-spinal fluid is very slightly raised in some cases. The levels of glucose and chloride in the fluid are both normal. During the first week of paralysis, a high cell count is still present. Later, there is gradual diminishing in the number. The protein content during this period tends to rise and is frequently up to 60 mg. per cent towards the end of this week. Almost all workers report increase of globulin in the cerebro-spinal fluid and it frequently remains positive until the fourth week.

There are certain diseases which might stimulate poliomyelitis. In the pre-paralytic stage, upper respiratory infection and influenza may be confused with incipient polio. It may be necessary to observe the patient closely over a period of time before polio is ruled out. During the stage

of meningeal irritation, it might be mistaken for cerebro-spinal or other forms of meningitis. Examination of cerebro-spinal fluid however will help in establishing the diagnosis. Encephalitis following a virus infection produced a clinical picture which closely simulates polio of the upper level type. A recent history of measles, mumps, chicken-pox or vaccination against smallpox should arouse in one a strong suspicion of an encephalitis. Disorientation and convulsions with spasticity of the extremities also aid in identifying encephalitis. The cerebro-spinal fluid findings are similar to those of polio except that in encephalitis. Sugar content is usually increased. Probably the most valuable differential point as regards encephalitis is the character of the drowsiness of the patient. The patient with polio when aroused is unusually alert and completely orientated. Sometimes it may, however, be almost impossible to differentiate polio from other virus encephalitis. Post-diphtheritic paralysis occasionally offers more difficulty in the diagnosis of polio. Diphtheria, however, is characterized by an acute membranous tonsillitis or pharyngitis which precedes the paralysis by a period of 7 to 10 days. The paralysis frequently involves the palate, but it may also involve other motor nerves. The patient is usually afebrile at the time paralysis occurs.

Outcome in polio

The prognosis in polio is more favourable in children under three years, and in adolescents over 15 years. Complete recovery is rare if paralysis has once set in. Though recovery may be nearly complete, there may be some region in which permanent muscular atrophy persists. From this condition of nearly complete recovery to one in which there is not the slightest recovery from the initial paralysis, there is every gradation. The prognosis is not influenced by the severity or otherwise of the general symptoms, for paralysis may be severe and may be extensive where the general symptoms are slight. The mortality rate varies with different epidemics. The rate is higher usually when the epidemic strikes a virgin soil. In the recent epidemic in Car-Nicobar Islands the mortality rate was 17.7 per cent.

Treatment of polio

The treatment of polio calls for a high degree of medical knowledge and skill and often requires the combined effort of general practitioners, health officers, children specialists, orthopaedic surgeons, neurologists and physiotherapists. There is no room for self-treatment or quackery in the treatment of paralysis.

As far as possible polio cases should be treated in a hospital, as expert nursing is required, particularly during the acute stage of the disease. In this stage absolute rest in bed is essential. The bed should be provided with

fracture boards to prevent sagging. Another board can be used across the bed for supporting the feet and preventing foot drop. Physical activity of any form in the pre-paralytic stage increases the severity of subsequent paralysis. This is due to reduction of resistance of the nerve cells to the virus. Hence not only should the patient be allowed to have any active movement in the bed but the spasm of the muscle should be treated. Hot packs are advocated to relieve muscle spasm. Recently curarine has been tried for the relief of muscle spasm in polio. This drug should be administered with very great care as it might produce respiratory paralysis, hence its use should be restricted to hospitals only. Private practitioners should on no account attempt to treat cases of polio in patients' homes with curarine as it will not be possible to keep them under constant observation. Another drug which has been tried in South Africa for the relief of muscle spasm is etamone. This drug is given intravenously or intramuscularly. Seven to 20 mg. per kg. of body weight is the dosage recommended. When the spasm is present, it is advisable to administer the drug three times a day. The treatment should be continued as long as the spasm and pain persist. The spasm is probably due to sympathetic over-activity resulting in heightened muscle tone. Etamone relieves spasm of pain probably due to its action upon the sympathetic. *It should be remembered that the above-mentioned drugs are not in any way specific for polio.* They can relieve only one symptom namely spasm. Hence in all those cases of polio where there is neither spasm nor pain, these drugs are not indicated.

Once the paralysis has set in, the treatment in the main, besides giving rest, should be directed towards preventing deformity caused by paralysis or spasm. In all cases of paralysis of pharyngeal muscles, where there will be difficulty in swallowing, the foot of the bed should be elevated in order to obtain postural drainage. Turning the patient on his face aids drainage. If there is difficulty in swallowing, nasal feeds may have to be given. In mild bulbar cases with respiratory embarrassment, oxygen will be of great value. When respiratory paralysis occurs, artificial respiration should be resorted to. As, however, ordinary manual methods of artificial respiration cannot be maintained, the patient will have to be treated in a respirator, or what is called 'iron lung'. The whole body of the patient is kept inside a metal box, while the head protrudes through a flat soft rubber diaphragm, which makes an air-tight shield about the neck. By means of electrically-driven blower and a valve arrangement, the air pressure within the tank is alternately changed from a few centimetres of negative pressure to a lightly positive pressure automatically simulating respiration. The rate, as well as the depth of respiration, can be

regulated. The apparatus should be used most frequently, particularly in those cases in which there is only mild or moderate weakness of the respiratory muscles. In such instances the respirator permits the muscles to rest, and recovery may be very rapid and more complete.

Orthopaedic treatment should be instituted as soon as diagnosis of polio is suspected. As stated before, rest is the one great essential in the immediate cure. This must not only be complete and absolute, but must be managed so that muscles placed at rest will be kept in a position of neutral muscle pull. This is the main factor in the prevention of later deformities. Deformity is preventable. In order to achieve this end, muscles must be protected from stretching and fatigue. A muscle placed at rest in a position of relaxation, with its attachments brought as close together as possible, will recover sooner and more completely than will one under tension. Under no circumstances are massage, exercises or electrical stimulation to be used during the early acute stage. Miss Kenny of Australia advocates hot packs during the early stages, gentle passive exercises and active movement. Excellent results are claimed with this method. However, it would seem that many of the movements that the patient makes during the demonstration period are of questionable practical value. Many of these functional activities that are permitted may be causing harm that will not show up until later. With the onset of paralysis splinting should be done. The purposes of splinting are :—

- (a) to balance muscles and thereby to retain neutrality of muscle pull;
- (b) to protect weakened muscles; and
- (c) to support limbs or other parts of the body.

Such position of the limbs should be maintained as are most desirable for future usefulness. Fingers and thumbs should be in the position of holding a drinking glass. Wrist should be in dorsiflexion. Forearm should be supinated 75 per cent. Elbow should be flexed to a right angle. Shoulder should be in abduction and part of the time in external rotation. Back should be straight or slightly elevated in the thoracic region. Hip should be abducted in 15 to 20 degrees of abduction without flexion or rotation. Knee should be flexed in 5 to 10 degrees. Foot should be at right angle without inversion or eversion. Head and neck should be straight without flexion or extension. Abdomen should not be allowed to become pendulous.

After the acute stage of paralysis, the affected parts should be immobilized either to correct deformities or to maintain normal position and keeping the joint from becoming over-stretched. The lower limbs are most frequently affected and are easily cared for in single casts or in bilateral plaster casts having a cross bar to prevent

Made by a new process to extremely fine dimensional limits, the barrel and the plunger produce such a complete seal between them that extreme care is necessary in removing minute particles of dust or other foreign matter before fitting the parts together. The syringe is made of low expansion heat-resisting glass which withstands sterilization of 300°C.

FIRST WOMAN DOCTOR

(Reprinted from Release No. B.F. 1332 issued by the British Information Services, New Delhi)

SUSSEX antiquarians want to preserve the house at Hastings where Britain's first woman doctor worked for 30 years. The house, a Regency building, was damaged by bombing.

On the house is a tablet which reads: 'Here lived and worked for 30 years Dr. Elizabeth Blackwell. Born at Bristol in 1821, she died at Hastings in 1910. The first woman to graduate in medicine in the United States in New York in 1849. The first woman to be placed on the British Medical Register in 1859'.

Her house, overlooking the English Channel, has been empty for 20 years.—L. P. S.

NEW TREATMENT FOR WHOOPING COUGH

(Reprinted from Release No. B.F. 1370 issued by the British Information Services, New Delhi)

If the experiments now being conducted in Britain are successful, 'high altitude' cure for whooping cough may become the standard hospital treatment for this complaint. The principle is not new, but as few hospitals are equipped with aeroplanes for high altitude therapy, this treatment has not been much employed.

The apparatus now being tried is a decompression chamber once used in the training of air pilots. It gives controllable air pressures corresponding to various heights.

Already encouraging progress has been reported. One six-year-old girl ceased coughing or vomiting only four days after this new treatment.

CENTRAL COMMITTEE ON SOIL SCIENCE

(From the Press Note dated 18th June, 1949, issued by the Press Information Bureau, Government of India, New Delhi)

THE Government of India in a resolution published in the latest issue of the *Gazette of India* have decided to appoint a Central Committee on Soil Science with a view to guide and co-ordinate the scientific study of soil in the country which is essential to put agricultural production on a planned basis. Composition of soil, its depth, its nutritional properties, mineral and moisture contents, etc., play a large part in intensive cultivation schemes which aim at producing the maximum out of the soil without impairing its fertility in any way.

FUNCTIONS

The functions of the Committee will be :—

- to advise the Government of India on matters of soil research and soil surveys;
- to guide and co-ordinate the scientific study of soil so as to ensure that soil survey proceed on right lines;
- to lay down the lines of soil survey to be followed for purely scientific and specific utilitarian purposes, and soil survey training;

to preserve in a central place the soil profiles representative of various types of soil;

to provide for the interchange of information and samples regarding soil types amongst the workers within the country as well as in foreign countries.

MEMBERS OF THE COMMITTEE

The Committee will be composed of :—

1. Dr. J. N. Mukherjee, Director, Indian Agricultural Research Institute (Chairman).
2. Dr. Dalip Singh, Principal, Government Agricultural College, Amritsar.
3. Dr. J. K. Basu, Soil Physicist, Government of Bombay.
4. Mr. P. D. Karunakar, Agricultural Chemist, Government of Madras.
5. Dr. R. C. Hoon, Officer on Special Duty, Central Waterpower, Irrigation and Navigation Commission.
6. Dr. B. K. Mukherjee, Director, Sugarcane Research Station, Shahjehanpur, U. P.
7. Dr. A. T. Sen, Soil Conservation Officer, Ministry of Agriculture.
8. Soil Survey Officer of the Indian Agricultural Research Institute (Technical Secretary).

The Committee will function under the Central Ministry of Agriculture. Soil profiles from various provinces and states will be preserved at the Indian Agricultural Research Institute, New Pusa, and the work on the preparation of soil maps of India, according to the lines laid down by the Committee, will be entrusted to the Institute.

'HIGH ALTITUDE' CURE FOR WHOOPING COUGH

A SERIES of experiments which has already met with considerable success is being conducted by Dr. H. Stanley Banks and the nursing staff of Park Hospital, London. With the aid of a de-compression chamber, as used by Battle of Britain pilots for training in high altitudes, child patients are given all the sensations of flying at about 12,000 feet when the atmospheric pressure in the chamber is gradually lowered. The 'descent' takes another 22 minutes. This is the first British hospital to instal such a machine for this purpose. A nurse enters the compression chamber with two young patients.

TUBERCULOSIS IN INDIA

(Abstracted from the *Chronicle of The World Health Organization*, Vol. 3, No. 2, February 1949, p. 23)

THE report of the Bhoire Committee revealed that about 500,000 people die annually from tuberculosis in India. This means that the annual number of cases is approximately two and a half to three million out of a population of 320 million.

The main reasons for this high* morbidity rate are threefold: bad housing, lack of sanitation, and malnutrition.

*The tuberculin negative rate of Delhi under the present highly unsatisfactory standard of living, caused by exceptional circumstances, does not appear to be unsatisfactory. For presumption of death and morbidity from tuberculosis see this journal, June 1949, p. 271. Villages presumed to be devastated by tuberculosis were really in the grip of kala-azar.—Editor, I.M.G.

POSSIBLE MEASURES OF CONTROL

The question is: what measures are possible? Hospital accommodation is quite inadequate.

In view of this situation, the authorities have turned their attention to prevention of the disease by BCG vaccination, in the hope of reducing the problem, within a number of years, to such proportions as to bring its control more within the financial possibilities of the country.

There were, nevertheless, great difficulties in the way of a BCG vaccination campaign in India. The first requirement was tuberculin for large-scale tests; this was not available in India and would have to be imported. Secondly, there was no institute in Asia capable of producing BCG vaccine. Thirdly, there was no trained personnel in India.

TECHNICAL ASSISTANCE BY WHO

To overcome the difficulties, the Government of India requested aid from WHO, and in response to this, Dr. W. Gellner and Dr. P. Lind were sent to India to set up a BCG laboratory and to demonstrate BCG vaccination on a mass scale. The first discussions took place with the Central Government and with Dr. P. V. Benjamin, tuberculosis adviser to the Government of India.

Financial difficulties seemed to stand in the way of an early implementation of those plans; they were, however, overcome by the readiness of the Central Government to contribute half the cost of the campaigns in the different provinces.

All the many articles of equipment—from incubators and analytical scales to filter-paper, ampoules, boxes and labels—were purchased and shipped to India. The shipments landed in India very shortly after Dr. Gellner's and Dr. Lind's arrival there, which made it possible to set up the laboratory in the King Institute at Guindy, Madras, in the record time of a few weeks. Production of the vaccine actually started about the middle of July and the first Indian BCG vaccine was available on 17th August, 1948.

The all-India BCG vaccination campaign was officially inaugurated in Madanapalle, South India, on 11th August, 1948, by the Indian Minister of Health, Rajkumari Amrit Kaur. From 1st August to 20th October, 1948, approximately 6,000 persons mostly school-children were tuberculin-tested and the negative reactors (about 2,000) received BCG vaccination. Twelve doctors from different parts of the country had been trained in the theory and practice of BCG vaccination.

The work in Madanapalle which aims at the vaccination and mass radiography of the total population, was taken over by an Indian doctor when Dr. Gellner left, towards the end of October 1948, for Delhi to start a second demonstration centre there.

In Delhi, between the end of October and 18th December, 1948, over 10,000 persons were tuberculin-tested and over 5,000 received BCG vaccination; while three doctors were trained in the work. The school-children, who formed the greater part of the tested and vaccinated persons, were dealt with in their schools, while two clinics—one in Delhi and the other in New Delhi—were established for the pre-school children and young adults.

The co-operation which the WHO team gained both in official quarters and among the general population was very good and augurs well for the success of the more extended campaign which is to begin now with the aid of the United Nations International Children's Emergency Fund (UNICEF). This organization—in agreement with WHO—is sending six BCG teams, together with the necessary transport and equipment, to India, where they will be distributed among those capital cities which have already made some preparations for this work.

The function of the UNICEF teams will be to train Indian doctors in the requisite techniques. So long as the Indian health authorities can provide a sufficient number of doctors to work with the foreign teams and to carry on and enlarge their work after the latter have left, it is to be hoped that a systematic BCG campaign will, in the course of time, materially affect the incidence of tuberculosis in India.

PRESENT STATE OF POPULATION GROWTH

(Abstracted from the *Chronicle of the World Health Organization*, Vol. 3, No. 2, February 1949, p. 33)

In a recent article in the *Epidemiological and Vital Statistics Report*, 1948, 1, 332, Mr. K. Stowman has reviewed the state of the world's population. On the basis of data now available, there can be little doubt that the population of the world has increased more rapidly in the twentieth than in the nineteenth century, and the rate of growth is still increasing. In the middle of 1946, the world population was estimated at 2,294,432,000 by the Statistical Office of the United Nations; in 1907, it was estimated at 1,606,000,000, and in 1882 at 1,434,000,000.

BRITISH JOURNAL OF UROLOGY

IN March this journal reached its twenty-first year of life, and the first number of the new volume appears in a very attractive style. It is now published by Messrs. E. and S. Livingstone Limited, Edinburgh, and edited by Mr. David Band who has succeeded Mr. Winsbury-White. The journal is published quarterly and the subscription rate £2-2-0 per annum.

FOOD AND MANURE

(Abstracted from the Independence Day Message of H. E. Shri C. Rajagopalachari, Governor-General of India, dated 3rd August, 1949)

I HAVE already expressed my concern and made my appeal about food and manure. It is our immediate and most important national programme.

annam brahmeti vyajaanaat अन्नं ब्रह्मेति व्यजानात्
 annadeva khalvimaani अन्नादेव खल्विमानि
 bhuutaani jaayante भूतानि जायन्ते।
 annena jaataani jivanti अन्नेन जातानि जीवन्ति
 annam prayantyabhisamvi-cantiiti अन्नं प्रयन्त्यभिः संविशन्तीति॥
 annam na nindyaat tad-vratam अन्नं न निन्द्यात् तद्व्रतम्।
 annam na parichakshiita tad-vratam अन्नं न परिचक्षीत तद्व्रतम्।
 annam bahu kurviita tad-vratam अन्नं बहु कुर्वीत तद्व्रतम्।
 no kanchana vasatau pratyachakshiita tad-vratam न कंचन वसती प्रत्याचक्षीत तद्व्रतम्॥

These verses are from our ancient scripture. The lines mean: From food are born all beings in this world and by food do they live, and, after death, they become food again for other beings. Food is indeed *Brahman*. We should not speak ill of food.

We should not throw away food. We should produce plenty of food. Let no one be turned away who comes hungry. This is most ancient wisdom and as valid now as in the old days.

SYNTHETIC CHLORAMPHENICOL (CHLOROMYCETIN)

(Abstracted from the *British Medical Journal*, 16th April, 1949, p. 672)

CONTOULIS, Rebstock, and Crooks have recently synthesized chloromycetin, to which the name chloramphenicol has now been given. Encouraging results have been obtained in typhoid fever, typhus fever, scrub typhus, and Rocky Mountain fever. The synthetic product, the structural formula of which is here shown, is (1) γ -1 *p*-nitrophenyl-2-dichloroacetamidopropane-1:3-diol; it has apparently the same physical and chemical properties as the chloramphenicol produced by the mould *Streptomyces venezuelæ* n. sp.

[In this connection also see page 369 and Editorial on chloromycetin in this journal, November 1948, p. 517.—EDITOR, *I.M.G.*]

DRUG RULES, 1945

(No. F.1-14/49-D., Government of India, Ministry of Health, New Delhi, the 22nd July, 1949)

THE following draft of a further amendment to the Drugs Rules, 1945, which it is proposed to make in exercise of the powers conferred by section 33 of the Drugs Act, 1940 (XXIII of 1940), is published, as required by the said section, for the information of all persons likely to be affected thereby and notice is given hereby that the draft will be taken into consideration on or after the 30th October, 1949. Any objection or suggestion which may be received from any person with respect to the said draft before the date specified will be considered by the Central Government.

DRAFT AMENDMENT

In Schedule H to the said Rules, to the entry beginning with the word 'Para-aminobenzene-sulphonamide' and ending with the words 'their salts' the following shall be added, namely:—

'But excluding preparations and dressings containing these for external use'.

(Sd.) J. N. SAKSENA,
Under Secretary.

WORLD CENTRE FOR MEDICAL RESEARCH

(Abstracted from Release No. B.F. 1488 issued by the British Information Services)

A NEW centre, the only organization of its kind in the world, has been opened in London for promoting international co-operation in medical and chemical research.

The ceremony was performed by Sir Henry Dale, President of the Royal Society of Medicine, who fully endorsed the aims of the centre, and said that he hoped that discussions and consultations would be planned on as widely an international basis as possible. He also looked forward to scientists and medical experts from Eastern Europe taking part in the various activities. It was essential that co-operation between doctors and chemists be promoted on a world-wide scale, for the benefit of humanity.

Lord Horder, Physician to the King, described this new venture as an international forum of research unknown in the world before.

LEPROSY RELIEF IN INDIA

(From the Press Note dated 2nd July, 1949, issued by the Press Information Bureau, Government of India, New Delhi)

THE Annual Report of the British Empire Leprosy Relief Association (Indian Council) for 1948 which has just been published reveals that the work of the Association has generally been maintained at a satisfactory level.

The Government of India have decided to give effect to the recommendation of the Bhore Committee Report regarding the establishment of an All-India Leprosy Research Institute. The Institute, when founded, would be able to make in due course a valuable contribution to the solution of the problems related to leprosy and its control in this country.

Another event of importance was the second session of the All-India Leprosy Workers' Conference, held at Calcutta, which was presided over by the Health Minister, the Hon'ble Rajkumari Amrit Kaur.

Dr. Dharmendra, Research Officer of the Association, spent eight months on a study tour in various parts of the United States of America, Mexico, Argentine, Brazil, the United Kingdom and Nigeria in West Africa, and gained useful experience of their leprosy and anti-leprosy organizations.

The research work of the Association has as usual been carried out in collaboration with the Endowment Fund of the School of Tropical Medicine at Calcutta and the Indian Research Fund Association. An important item of research has been the continued studies on the therapeutic value in leprosy of the new sulphone drugs; study of the correlation of histological and immunological findings with the subsequent course of the disease in selected cases and a study of nose and throat lesions in leprosy.

A new film entitled 'Our Duty' has been completed and is ready for projection. This is a two-reeler talkie film and will form a very important addition to the Association's anti-leprosy publicity material.

The Association took part in the Sarvodaya Exhibition organized in connection with the Session of the Indian National Congress held at Gandhinagar, Jaipur.

The provincial reports indicate that steady progress is being made in the Association's activities in the provinces. The various activities, such as treatment, propaganda, teaching in medical institutions, surveys, etc., have been continued. The important question of isolation of infective cases of leprosy received increasing attention during the year under review.

NEW DEVICE FOR CANCER TREATMENT

(From Release No. B.F. 1528 issued by the British Information Services, New Delhi)

THE first medical synchrotron to be built in Britain has just been completed at the Royal Cancer Hospital, London, and will be used in an important new series of experiments.

It is believed that the machine will produce rays sufficiently powerful to reach the deepest cancer growths since they are 12 times more penetrating than the x-rays used hitherto for cancer treatment.

The synchrotron has been developed under the guidance of the Atomic Research Establishment of the Ministry of Supply.

Public Health Section

ACTIVITIES OF INDIAN ANTIMALARIA UNITS IN WORLD WAR II

By C. P. NAIR

(lateLY MAJOR, M.B.E., I.M.S./I.A.M.C.)

NUMEROUS instances can be cited to show that malaria has caused more casualties than weapons of war in many an army. During World War II, few people would realize that in 1943, for every single fighting man put out of action by the Japanese, 121 were incapacitated by sickness mainly due to malaria. In 1944, when fighting was severe, the ratio of casualties was still 1 to 19. There is ample evidence to show that the ratio was again considerably reduced during the year 1945 to 1946. That the activities of the Indian antimalaria units played an important rôle in the victory of the Allied Forces, especially in the Eastern theatres, is obvious. The experiences of the writer, while working as the officer commanding two antimalaria units, form the subject-matter of this paper.

The antimalaria unit is an independent medical unit designed for the control of malaria and for the investigation of its carriers. During the war, an antimalaria unit consisted of the following staff, supplemented by civilian labour whenever required.

Commanding officer (commissioned officer) ..	1
Indian other ranks (including 1 V.C.O. and 8 non-commissioned officers) ..	18
Non-combatants enrolled (including a tinsmith) ..	55

Work in Bhiwandi

The writer was placed in command of a unit which was raised at Babina in August 1943. This unit was allotted work in military camps, some inside and others outside the Salsette island, Bombay area, with headquarters at Bhiwandi. It may be mentioned here that Bhiwandi Camp was known in military circles as one of the highly malarious camps and men feared the mosquito assault more than that of the cannon. The population in that camp at the time of the arrival of the writer with his unit was about 10,000. The camp was located at the foothill region, about 2½ miles from the town of Bhiwandi and surrounded on all sides by thick forest, from which the camp derives its name. The villages adjoining the camp within a radius of a mile are Binar, Nimboli, Kasoli, Damango, Vadpa, Borivli, Panjrapur, with spleen rate among children ranging from 40 to 90 per cent. Four more important camps (Pokran, Mulund, Vada and Bhiwandi Bakery

Camps) were also in charge of this unit. All of them without exception were extremely malarious.

Control measures.—Writer's enquiry into the incidence of malaria in the area, especially Bhiwandi Camp, started with study of the figures of admissions for malaria in the local combined (European and Indian) military hospital. This was approximately 5 per 1,000 per day which is a very high figure. Since the incidence of malaria was high and control work had to be pushed through as vigorously and as quickly as possible, much time could not be devoted for carrying out elaborate surveys. So a quick and rapid survey was carried out in two days into the malariogenic features of the area involving spleen, parasite, mosquito (both larval and adult) surveys, employing all the men for the purpose. The surveys indicated the presence of *A. fluviatilis*, a well-known and active carrier of the foothills of the Indian region, in appreciable numbers in houses, as well as larvæ in slow-flowing, sunlit and unpolluted streams and channels with marginal vegetation. The area requiring control was about ten square miles. The immediate control measure suggested itself after the survey. Spraying with pyrethrum insecticide had to be done to kill all the adult *A. fluviatilis* mosquitoes resting in the camps and also surrounding the villages within a radius of a mile, before they became infective (*vide* figure 1, plate XXIV). So systematic spraying was done from the beginning of September till the end of November, with 0.1 per cent pyrethrum for six days in the week during the early hours of the morning so as to destroy the sluggish adult mosquitoes after their rather heavy blood meal during the previous night. The sickness rate fell considerably after the spraying and this amply repaid the high cost involved in carrying out the campaign.

After this preliminary control measure, which the conditions prevailing at the camp at the moment urgently called for, other antimalaria methods were carried out according to feasibility. The breeding places, especially the vectors, were carefully noted and signboards (figure 2, plate XXIV) were put up to show the control staff that adequate measure should be taken. Antilarval work with malariol, using knapsack sprayer at approximately 15 gallons per acre for streams and large pools, mopping with a brush soaked in malariol for rock-edged pools, streams and channels was done. Drip cans were used for controlling mosquito breeding in small channels and oil *guddas* in pools and underneath road culverts. Dusting with paris green (1 per cent in soapstone powder) was employed for destroying anopheline larvæ in the

marshes in the vicinity of the camp using approximately 1 pound per acre.

The area requiring control having been well studied, it was possible to divide it into four sections for better organizations of the work, each in charge of a non-commissioned officer with 12 men under him. The men in each of these sections were responsible for all types of antimosquito work. For antilarval work, the area comprising a section was divided into six divisions, corresponding to six working days of the week. Sunday was utilized for maintaining the equipment in good working condition. At this time a 'check up' of the control measures was developed by the writer and is described below.

The efficacy of the control measures was checked by making collections of larvæ and adult mosquitoes (figure 3, plate XXIV). Since conclusions regarding the efficacy have to be mostly formed on the collections made by the man deputed for the work, it was necessary to select a man specially suited for this purpose. After the selection of a suitable man, it was still found necessary to obviate personal bias. This was arranged by deputing a mosquito collector of one section to collect in another section according to a fixed routine programme. Efficiency in this checking work was further increased by the institution of a prize based on a system of awarding marks for the collections—one mark for a non-vector mosquito adult or larva caught, and five for vector species. Similarly, individual prizes were distributed every month to the men in the section from whose area minimum number of marks were scored by the corresponding mosquito collector. It can be inferred that in the section wherefrom mosquitoes were caught, the control work was poor. So inspection by the writer was made immediately in that section and the defect rectified. By this means, healthy competition between the four sections was created and it is needless to mention that it increased very much the efficiency of the antimalaria campaign as a whole.

A field laboratory, for receiving the collection of adult and larvæ of mosquitoes, studying them, classifying them into various species according to their breeding habits, dissecting the adult mosquitoes, compiling the proportion of males and females, for examining blood films for parasites, and classifying them, etc., was set up and the work in the laboratory and in the field was thus co-ordinated into a regular routine which is very essential for any sound antimalaria campaign. As a result of these studies, two species of mosquitoes, *A. jeyporiensis* and *A. jamesi*, which were not previously recorded in the area, came to be recorded (Covell and Puri, 1936).

For educating the officers and men in the camp to develop a high malaria conscience, which would greatly help antimalaria work, a permanent malaria museum was set up con-

sisting of charts, specimens, exhibits of equipment, etc. All the unit squads were trained in basic principles of antimalaria work for about a week. General lectures on malaria and its investigation and control were periodically arranged for the benefit of the troops.

Antimalaria campaign was further strengthened by making the officers commanding both medical and non-medical units in the area responsible for all antimalaria measures inside their unit lines. These measures were regularly supervised by the writer. When two or more units occupied an area, the officer commanding the largest unit was responsible to co-ordinate the antimalaria measures in that area.

Each unit had an antimalaria officer (non-medical man) to whom all necessary assistance and advice were given by the writer. These officers had an antimalaria squad under them based on 4 per cent strength of their unit. These squads were in turn under the supervision of really good non-commissioned officers and the men in the squad were permanently appointed for doing antimalaria work.

The unit antimalaria officers were made responsible to divide their areas into six sub-areas and show them on a sketch and exhibiting the unit offices. The unit squads worked in each area one day in the week.

Measures of personal prophylaxis such as the proper dresses during the evening and at night, the proper use of nets, antimosquito cream and repellents, were all regularly enforced and maintained at a high level of efficiency. These measures consisted of:—

(i) Wearing trousers, long sleeved shirts fastened at wrist, boots and anklets after sundown by all ranks until they get under their nets.

(ii) A sunset parade in all units for the inspection of antimosquito clothing, and the application of antimosquito cream to the face, neck, hands and other exposed parts of the body. As one application of antimosquito cream protects only for about 2 hours, guards under the unit arrangements were to give gong or whistle 2 hours after sundown for the re-application of repellent by all ranks who were not inside mosquito nets. Similarly, an interval was arranged in the camp cinemas for re-application repellent supervised by a senior officer present.

(iii) Recreational bathing (i.e. other than ablution purposes) between dusk and sunrise was strictly forbidden.

(iv) Use of mosquito nets throughout the night by all ranks not on duty. Night guards or special patrols organized by units patrolled all barracks and sleeping quarters and ensured that mosquito nets were rendered effective throughout the night by moving away men from their nets or tucking in nets without the men being awakened.

(v) Placing out of bounds between sunset and sunrise all villages and local habitations.

During the second year of the author's stay, extensive antilarval measures were carried out, such as filling potential breeding places, trimming the edges of breeding places, removing jungle which cannot give complete shade to inhibit *A. fluviatilis* breeding, large-scale canalization, re-channelling, widening of hill streams (figure 4, plate XXIV); digging of drains, central and contour, to drain away the swamps and storm water quickly; construction of a fair number of semi-permanent dams and sluice gates (figure 5, plate XXIV) to furnish the water in the hill streams periodically to wash the larvæ away from the site of the camp. These sluices were either made from 40-gallon oil drums closed with a wooden shutter or made of wooden frames somewhat similar to those of a window with a shutter also made of wood working in a groove in the frame work. The different types of breeding places dealt with the above described measures, especially in Bhiwandi Camp, were :—

1. Tortuous hill streams about 40 miles in length.
2. Seepage water stagnations in the foothills.
3. Extensive swamps.
4. Borrow pits.
5. Fallow paddy fields.

During the transmission season, DDT was employed for residual spray with stirrup pumps, instead of pyrethrum. Even for antilarval work, DDT was widely employed. Once a week spraying with DDT 5 per cent solution in malariol was done with knapsack sprayers, spraying at intervals of 5 to 11 paces depending upon the breeding place. Other methods used especially in swampy sites were the distribution of 'bhusa' and sand soaked for 24 hours in DDT solution, using approximately 0.1 pound of DDT per acre. A form of sprinkler made from tin containers and having 4 or 5 small holes so small as to deliver the liquid in drops was used, using 4 drops per square yard or 4 cc. per 10 square yards.

Control measures were chalked out for adoption by units in their respective areas and these consisted of :—

(1) *Anti-adult measures*.—Spraying the inner and outer walls of all buildings and tents with 5 per cent DDT in grade III kerosene once a fortnight during the malaria season. As an antily measure, the floors of all kitchens, dining halls, canteens, latrines, refuse and swill bins and their surroundings were allowed to be sprayed once in two months. Spraying was asked to be done properly, paying special attention to the following points: (a) The operator should cover all the surfaces to be sprayed with a wet spray, thinly and evenly.

(b) The dosage of DDT that should be aimed at while spraying should be about 100 mg. per square foot, which is equivalent to 4 pints of 5 per cent DDT solution per 1,000 square feet. Equipments for spraying were issued to the units with the recommendations that :—

(i) Flit guns are not so very satisfactory for DDT residual spraying.

(ii) The average rate of discharge from a Mish sprayer is about 1 pint in $7\frac{1}{2}$ minutes and hence this is rather tedious for large areas.

(iii) Power sprayers are mainly meant for an atomized spray and therefore, for a wet spray, these are not very satisfactory. But in offices where charts and pictures are hung from the wall, power spray can be utilized with a limited scope. This should be taken into account.

(iv) The average rate of discharge from a knapsack sprayer is 1 pint per minute. A 20-inch rubber tubing fitted to a knapsack sprayer is considered the most handy and mobile form of apparatus.

(v) When spraying surfaces, the nozzle of the sprayer should be held at right angles to the surface at a distance of 12 to 14 inches away. If the rate of discharge and the surface areas to be sprayed are known, the dosages can be kept up by calculating the time required for spraying that particular area and adjusting the spraying according to that.

(vi) Stirrup pump fitted with knapsack sprayer nozzle is also a suitable apparatus for DDT residual spray. The man operating the stirrup pump should not pump very frequently, because due to high pressure, the rubber tubing is liable to burst. One stroke for every 20 counts is an average working rate of the pump.

(vii) Under normal working conditions, DDT is not toxic to man but still men spraying the solution should wear anti-gas eye-shields and gauze face masks and should wash with soap at the end of the day's work and before feeding.

(2) *Antilarval measures*.—(i) Reducing the surface area of water as much as possible by canalization, drainage, filling in pools and draining small pools into large ones.

(ii) Keeping clean the edges of all pools, streams and drains.

(iii) Applying DDT 5 per cent, or 1 per cent in malariol, roughly once a week, to the edges of all streams, drains, pools and all water collections.

The following methods of distribution of DDT for antilarval work were also recommended :—

(a) Mixing 15 pounds fine dry river sand with 1 pint of 5 per cent DDT in malariol and throwing by hand to all water collections.

(b) Mixing sawdust with DDT solution and applying as above.

(c) Applying 1 per cent DDT solution in malariol by mop and home-made bucket method.

(d) Using cigarette tin on a stick with a minute hole punched in the bottom.

(e) Forcing in DDT 1 per cent in malariol into all crevices by means of a sweeper's brush.

(f) Using knapsack sprayers or stirrup pumps and spraying 1 per cent DDT solution.

All units in the area were required to observe Saturdays as dry days. On dry days all fire buckets, grease traps, small water tanks and other receptacles holding water at their unit lines were emptied to stop larval breeding.

Results.—The results achieved by the campaign during the period when the writer was in charge of Bhiwandi Camp are furnished below :—

Malaria sickness

Year	Number per 1,000 per day	Spleen rate, per cent
1943	5.0	40-90
1944	0.5	10-60
1945	0.2	4-25
(till July 1945).		

Work in Malaya

The experiences of the Second Antimalaria Unit, which was also under the command of the writer, were altogether of a different type for various reasons. Type of work, the nature of the land, climate, conditions under which the unit had to function, were all different. This unit accompanied an Army Corps proceeding to Malaya for assault landing but this at the time of landing turned out to be a matter of re-occupation only. But the entire programme of antimalaria work that was expected of such assault landing was gone through. As soon as the antimalaria unit landed at Morib, Beack Klang District, Selangor, the antimalaria personnel started routine barrier spraying (figure 6, plate XXIV) of every inch of the space to be occupied by the troops and 50 yards belt all round, the men being equipped in advance while abroad with Mish spraying (pumps) guns and a gallon of DDT 5 per cent solution. After this preliminary control, other aspects of the work could be considered, such as the organization of the staff, surveys, studying the area thoroughly, planning of future control measures, etc.

The malaria problems of Malaya are very interesting and even at very close quarters there mosquito vectors could be located. They were *A. sudaicus* of the coastal area, *A. maculatus* of the foothill areas, and *A. letifer* of the inland plain breeding in shaded waters.

During the period September 1945 to June 1946, the headquarters of the unit and laboratory museum, etc., were located in Klang and the writer had the opportunity to study the various aspects of 'barrier spraying' as a

method of malaria control. Residual spraying with DDT 5 per cent solution in kerosene was systematically done in a village to learn about its utility as a rural malaria control in the local tracts (Nair, 1947a).

Towards the latter part of the stay in Malaya, DDT 'barrier' spray, which formed the chief means of malaria control till then, was gradually substituted by DDT residual spray once in six weeks, using 100 mg. per square foot and this was extended to all the houses for half-mile radius surrounding the camp sites (figure 7, plate XXIV).

In addition to the DDT spray, suppressive treatment with mepacrine (at the rate of 1 tablet per day) and personal protective measures were enforced regularly among the military personnel in Malaya.

It may be mentioned that as a result of the efficient work of the antimalaria unit, the sickness rate during the height of the transmission season in the camp was only 0.1 per 1,000 per day during the year 1945 (September to December), the period of high malaria incidence in Malaya in areas where *A. letifer* is the vector species.

Conclusion

The experiences and knowledge obtained in military campaigns are of considerable practical utility in civilian life. The discipline of the men in the military is very favourable for all types of malaria control. In fact, the military campaigns often give impetus to research and sometimes research has to be done, and done quickly, to ease particular situations. It is true of malaria control also. In malaria control, though actual control of the malaria is what is required, various procedures and methods are evolved which are more used in civilian life after the termination of hostilities. The author has had the opportunity of carrying out independent investigations on the various aspects of DDT 'barrier and residual spraying and on the bionomics of the local anopheline mosquitoes' (Nair, 1947b). These will, it is hoped, give valuable information to workers on

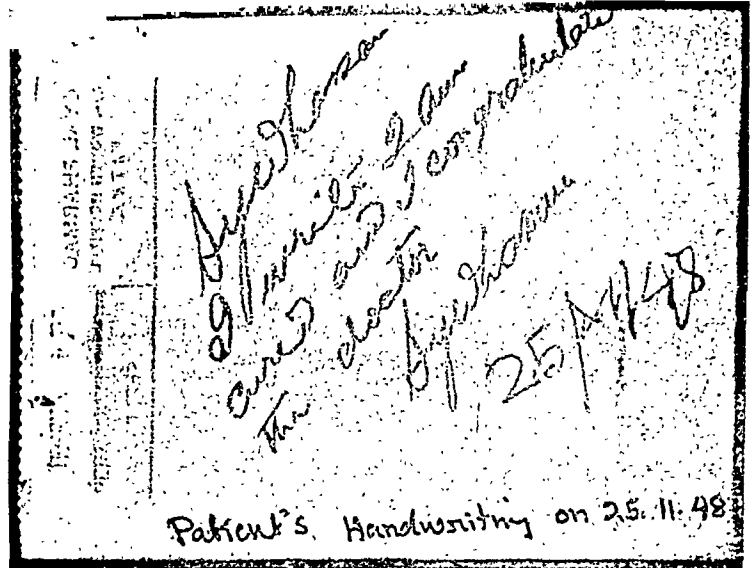
EXPLANATION OF PLATE XXIV

- Fig. 1.—Space spraying with pyrethrum insecticide.
 Fig. 2.—An insect collector collecting larvae from a typical breeding place. Note the signboard indicating the nature of the dangerous breeding place.
 Fig. 3.—One insect collector doing night catching from a village house. Note the syphon tube in use.
 Fig. 4.—Re-channelling and widening of hill streams.
 Fig. 5.—Flushing a small hill stream by means of semi-permanent dam and sluice gates.
 Fig. 6.—'Barrier spraying' squad at work in the field using Mish sprayers under the personal supervision of the officer.
 Fig. 7.—DDT residual spraying of a village house.

SYMMETRICAL GANGRENE : R.
SUBRAMANIAM. (O. A.) PAGE 334



A CASE OF PARKINSON'S DISEASE TREATED WITH
PARPANIT : R. K. SANYAL. (O. A.) PAGE 345



SUCCESSFUL REMOVAL OF AN ELEPHANTIASIS SCROTUM WEIGHING 70 LBS. (35 SRS.) IN A VERY POOR
SURGICAL RISK CASE : N. DAS & M. MUKHERJI. (M. H. P.) PAGE 347



Fig. 1.—Before operation.

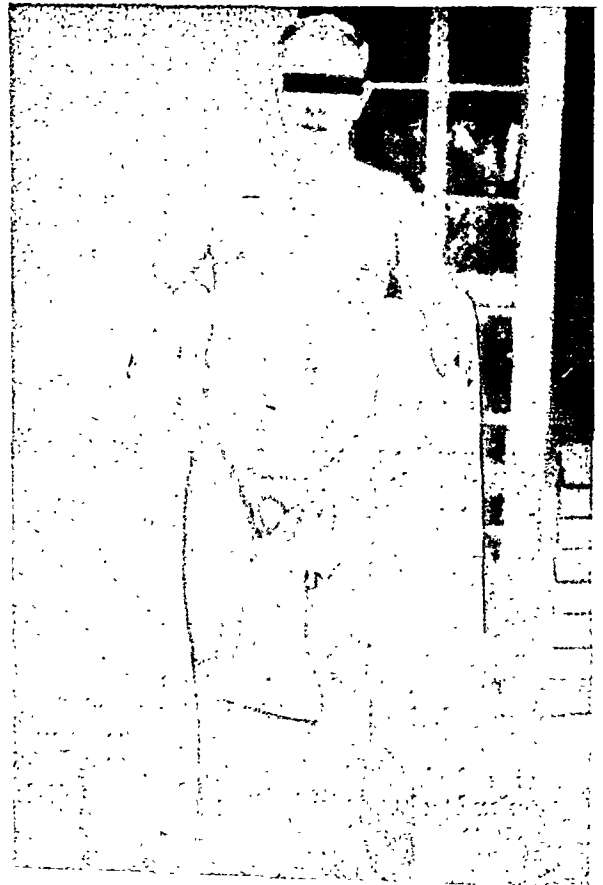


Fig. 2.—After operation.



Fig. 1.

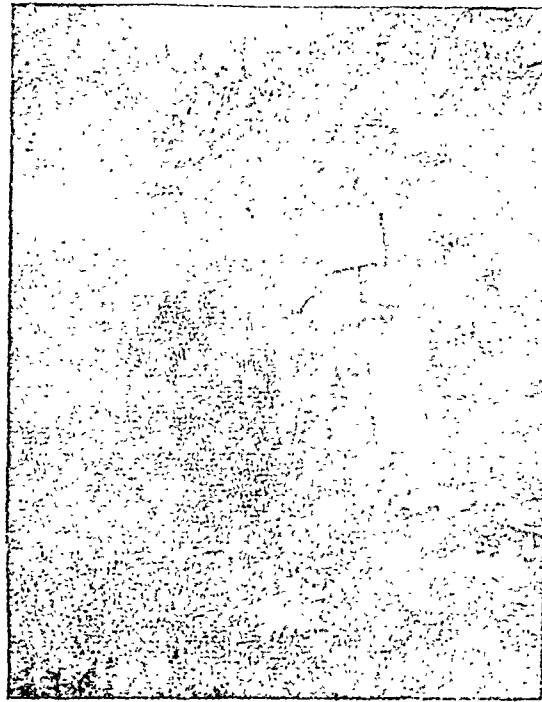


Fig. 2.



Fig. 2.

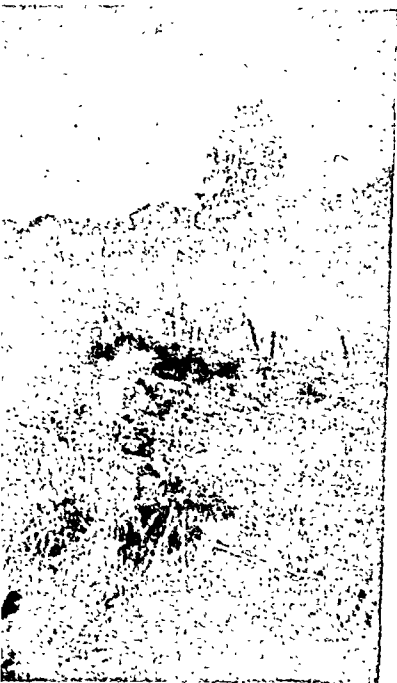
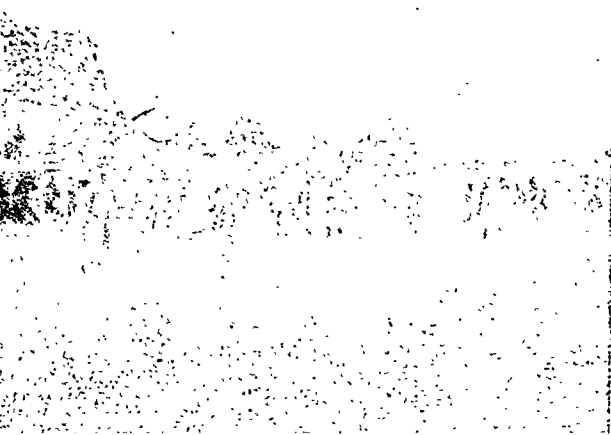


Fig. 4.



Fig. 5.



the subject. Also he has found that the method of antilarval control by using sand soaked in 5 per cent DDT solution is economical and effective wherever feasible. Similarly, several units working in remote areas have found new species of mosquitoes hitherto not recorded, such as the recording of *A. jeyporiensis* and *A. jamesi* in Bhiwandi by the author.

Such information adds to our knowledge on the subject. The recent war developed DDT as a weapon of outstanding merit in antimalaria work. It was originally used in Switzerland for the control of potato beetle and cloth moths. Considerable practical knowledge in the use of this insecticide for antimalarial work was gained during World War II though much still remains to be done.

The development of military antimalaria organizations for India during World War II was due mainly to the untiring efforts of many malariologists, especially Major-General Sir Gordon Covell, the then Director of Malaria Institute of India and Consultant Malariologist, India Command; Brigadier M. K. Afridi, Consultant Malariologist, South-East Asia Command; and Lieutenant-Colonel Jaswant Singh, the present Director of Malaria Institute of India.

The author wishes to record his grateful thanks to the Director, Medical Services of India, for his permission to publish this article.

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The Indian Medical Gazette Fifty Years Ago

DISEASES DUE TO SELF-EMPOISONING OR AUTO-INTOXICATION

(Reprinted from the Indian Medical Gazette,
August 1899, Vol. 34, p. 291)

THE leading trend of medical science of late years has been mainly in the direction of viewing disease—its causation, treatment and prevention—more and more from the chemical standpoint; of looking at most of the general diseases and functional nervous disorders as poisonings of the blood or toxæmias. This apparent swing of the pendulum of opinion back towards the old humoral doctrine that 'the Blood is the Life' is not in reality a retrograde movement, but an advance on a higher platform and represents the most modern development of medical progress.

It has long been recognized that some alteration in the quality of the blood appears to precede in a causal relation any alteration of structure by disease, and that a poisoned blood-supply means diminished health and life, if not actual death. But it is only just coming to be recognized how extremely prevalent blood-poisoning is as a prolific source of a host of ordinary ailments and diseases not hitherto suspected of being associated with it.

Whilst so many workers at the fascinating parasitic theory of the infectious fevers have been proving that the symptoms of such diseases are due in great measure to the poisonous chemical products, the toxins, of the malignant microbes which have invaded the body and which have to be combated by antitoxins; other observers have been investigating the effects of those bacteria, which are normally present in the body, and of those products of digestion and tissue-change, which, when disturbed by over-production or non-elimination, poison the blood and so produce multifarious disease. In this way, it is being found, are produced not only the ordinary so-called 'blood-poisoning', but innumerable diseases, such as apparently gout, rheumatism, neuralgia, headache, 'biliousness', and obscure feverish attacks including what is often termed 'a touch of malaria', and even such unexpected conditions as general paralysis and certain kinds of insanity. So far-reaching and widespread indeed are the effects of these auto-intoxications that the subject is well deserving of quite as much attention as is being paid to the infectious fevers, for it affects immediately the comfort and fate of a much greater number of human lives.

Strictly speaking, 'auto-intoxication' should be confined to that poisoning of the system by products elaborated by the individual's own living tissues, namely, by that class of chemical products which are called *leucomains*, such as produce gout, neuralgia, etc. It nevertheless is also usually held to include poisoning by absorption of the products of bacterial fermentation and putrefaction in dead matter, the so-called *ptomains*, which produce the familiar symptoms of septicæmia and infective and other fevers and irritant poisoning.

The former class, the *leucomains*, seem to produce poisoning through some alteration in the activity of the ductless glands which regulates tissue-change, whilst the *ptomains* resulting from the vital activity of bacteria, depend on excessive fermentation or putrefaction of the contents of the intestinal or other cavities or surfaces. Chemically, these *ptomains* are closely allied to the 'alkaloids', which, like them, are also produced by living plants, and whose poisonous action (as of nicotine, morphine, strychnine, daturine, etc.) has long been recognized as producing severe affections of the nervous system, such as stupor, convulsion, mania, insanity, etc.

As instances of poisonous leucomains are xanthocreatinin, which causes depression and vomiting, para-xanthin and heteroxanthin, which causes rigor and convulsions, gerontin, which paralyses the nerve-centres and ganglia of the heart, and from choline it has been shown by Schmidt and Weiss that poisonous neurine may be formed by the action of bacteria—the action of neurine agreeing closely with muscarine in paralysing the heart and purging, and in being especially toxic to nerve trunks, paralysing respiration like curare. The production of ptomains is chemically a process of oxidation with the formation of sulphuretted hydrogen, carbonic acid and water as by-products.

The range, therefore, of widely different process covered by auto-intoxication is very great. Although as yet but imperfectly understood, it would seem to include the following: Firstly, the processes by which toxins, which are stored up in the body as the result of some interference with the ductless glands which produce substances indispensable to healthy life, such as when the thyroid gland is congenitally absent or its function extinguished by tumour or extirpation, there results cretinism or myxœdema evidently as an auto-intoxication, and feeding such patients with the thyroid glands of sheep removes the symptoms; and if the same kind seems to be the action of citric acid in scurvy and iron in anæmia, by supplying the blood with certain deficient substances.

Secondly, those in which chemical products of healthy cell life, normally present in the blood, which become so increased by abnormal chemical activity or defective excretion, as to act as toxins such as certain products of digestion, choline, urea, causing uræmia, sugar in diabetes, acetonuria, sulphuretted hydrogen.

Thirdly, those in which abnormal products are the result of microbes, and especially of the putrefactive bacteria, which invade the gastrointestinal tract. Under this class comes septicæmia, and probably malaria, and also pathological products, which produce diabetic coma-albuminuria.

But it is through the intestines that auto-intoxication most frequently occurs by putrefactive changes in the food. Any undue delay there of the ingested food leads to absorption into the bloods of toxic ptomains, which poison the system and produce the train of symptoms, headache, feverishness, biliousness, etc. For this, although constipation or coprastasis is the rule, it also occurs in the fermentation of diarrhœa, dysentery and cholera.

The exact manner in which this auto-intoxication occurs is beginning to be ascertained. When fermentation of carbohydrates occurs, we have produced the various fatty acids, while with the decomposition of the albuminous substances, there result ammonia, sulphuretted hydrogen, indol and skatol, leucin and tyrosin,

and some other products. 'Aaron and others have shown that there is a constant formation of ptomains and toxins in the intestinal canal by bacterial action. The retention of all these injurious products would naturally, if absorbed—and experiment has proved that this absorption does take place—work harmful changes in all parts of the body. The nervous system being the most delicately organized is usually the first to suffer. While we do not know positively that such is the case, yet reasoning from the fact that a cleaning out of these poisons, i.e. of the intestinal tract, often causes a prompt disappearance of the symptoms, we have at least strong presumptive evidence. The kidneys, if not acting properly, are also a most important factor in the production of auto-intoxication. Bouchard states that in the normal urine of an adult man, there is present each day a sufficient quantity of several poisonous products to have caused the death of the individual, if not excreted. We can readily see from this how small an amount of kidney disturbance may be required to produce symptoms of auto-intoxication. Among nervous symptoms probably the most common is headache. Almost all of us are acquainted with the relief that follows a thorough evacuation of the bowels. Vomiting of the so-called cerebral type occasionally occurs. Among psychic symptoms, disinclination to work, depression of spirits are all of the most frequent occurrence. Among circulatory disturbances, may be mentioned tachycardia and other forms of vasomotor alteration. Skin affections are not uncommon as the result of auto-intoxication. The occurrence of urticaria as the result of the ingestion of certain foods, particularly lobsters, strawberries, and tomatoes, while at one time ascribed to idiosyncrasy, we now know to be due to auto-intoxication, for in so-called susceptible individuals, the urticaria has been prevented by keeping the intestinal canal free and active. Albuminuria may occur as a result of auto-intoxication: in the various forms of acute and chronic intestinal obstruction, the exit of toxins being prevented along the *prima via*, they are absorbed and finally excreted to a considerable extent by the kidneys, on which latter they exert their poisonous action. We can readily see that albuminuria might result, or even an acute nephritis. We must regard chlorosis as due to a large extent to auto-intoxication'.

The symptoms of general paralysis appear to be due in great part to auto-intoxication. Drs. Mott and Halliburton, in a paper recently (20th April) read before the Royal Society, show that choline ($C_5, H_{15}, N_{0.2}$) and nucleoproteid are produced by the acute disintegration of brain-tissue, and are absorbed into the blood. They found choline in the blood of general paralytic patients and ascertained its characteristic action on the neuromuscular mechanism of the blood-vessels.

* Jour. Amer. Med. Assoc., Jan. 1899.

The practical outcome of these investigations is already considerable. While broadly establishing on a scientific basis, Dr. Lauder Brunton's so-called 'internal sewage system' of treatment by internal disinfectants, such as salol, these observations indicate the lines of treatment in certain specific cases. Thus it would seem that in general paralysis and certain nervous states, where choline and neurine are produced, the use of food containing much lecithin, such as eggs, should be prohibited, as lecithin tends to split up into the two poisonous bases above mentioned. Even a thickly-coated tongue may load the blood with toxins. Diabetes, Dr. Lauder Brunton believes, may find its cure possibly in a glycolytic enzyme, although about a quarter of a century ago he failed to extract such a substance from muscle.

These attractive investigations are still in their infancy, and much care will be needed to avoid interpreting merely secondary results as causes. Altogether this field of research in chemical physiology is one of the most promising in practical medicine, and bids fair to yield results which will remove a large amount of discomforting illhealth and disease.

Current Topics, Etc.

Chloromycetin in Rickettsial Infections

(Abstracted from the *Lancet*, i, 19th June, 1948, p. 953)

THE efficacy of the antibiotic, chloromycetin, in scrub typhus, is likely to prove a discovery of capital importance. The first results of the Anglo-American clinical trial proceeding in Malaya suggest that we at last have a potent remedy for the rickettsial diseases. The antibiotic was isolated in 1947 by Ehrlich and colleagues in Detroit from a soil actinomycete, and its active principle, obtained in crystalline form, was found to differ from any antibiotic so far described in containing both nitrogen and non-ionic chlorine. In laboratory infections, chloromycetin, weight for weight, appeared more effective against *R. prowazeki* in chick embryos than any other agent tested under these experimental conditions, and large doses produced no symptoms in animals. These encouraging laboratory results demanded clinical trial in human typhus infection, and satisfactory results were claimed in a few cases of epidemic typhus in Mexico early this year. Since March, Smadel, and other research-workers from the U.S. Army and the University of Maryland, have been collaborating with Lewthwaite and Savor of Kuala Lumpur in a clinical trial in scrub typhus, and preliminary results were reported at the International Congress on Tropical Medicine at Washington, D.C., in May. So far 25 patients have been treated with the drug, while a control group of 12 untreated cases have been observed during the same period. The treated and untreated come from the same areas and in some cases from the same plantations, so the strains of *R. tsutsugamushi* are likely to be of similar virulence. The mean ages of the two groups—an important factor in any typhus infection—were the same. The diagnosis was proved in each instance, either by recovering the rickettsia from the blood or by demonstrating satisfactory titres for agglutination against an OXK strain of *Proteus*. In the treated group, no body developed complications or died; the average duration

of fever after the first dose was 31 hours, and the average total febrile period 7.5 days; one man, treated on the third day of the disease, was discharged for light work on the 9th day after onset. In the untreated group of 12, 2 patients developed serious complications and 1 of these died, while the mean duration of fever was 18.1 days. The chloromycetin was given by mouth, initially in large doses; but these were gradually reduced, and the last 7 cases were given the drug for only 24 hours, receiving a total of 6 g., with an equally satisfactory response. Half the patients were treated on estate hospitals where nursing conditions are necessarily somewhat primitive.

[In this connection also see page 362 and Editorial on chloromycetin in this journal, November 1948, p. 517.—*Editor, I.M.G.*]

Polymyxin and Aerosporin

(From the *Lancet*, i, 5th June, 1948, p. 875)

At one time it seemed likely that the two antibiotics polymyxin and aerosporin would prove to be identical, but it is now clear that they are distinct though related more or less as are the different penicillins. Both are active against many gram-negative organisms not much affected by other antibiotics, including *Bact. coli*, *H. pertussis*, *B. aerogenes*, *Br. abortus*, and some varieties of salmonella and shigella.

The production, isolation, and preliminary characterization of polymyxin were described nearly a year ago by Stansly and his colleagues, of Johns Hopkins, who obtained it from the fermentation liquor of *B. polymyxa*, a soil organism. In further experimental and clinical investigations, Schoenbach *et al.*, also of Johns Hopkins, have shown that it is active against gram-negative organisms in the presence of serum and that it does not give rise to resistant strains like streptomycin. This is also true of aerosporin. Unfortunately, the toxicity of both these antibiotics is considerably greater than that of penicillin or even of streptomycin. In the control of experimental infections in mice with *K. pneumoniae* and Pfeiffer's bacillus, polymyxin appeared to be five to ten times as effective as streptomycin. In total daily doses of 5 mg. per kg. of body-weight, given at intervals of three hours, polymyxin has been used to treat patients infected with *Ps. pyocyanea*, *K. pneumoniae*, *H. pertussis*, and *Br. abortus*. The antibiotic certainly has a therapeutic effect, but too few patients have been treated for its clinical value to be appraised.

Aerosporin, which has been studied in this country by a group at the Wellcome Physiological Laboratories, is derived from an aerobic spore-bearing bacillus identified as *B. aerosporus* Greer, which may be identical with *B. polymyxin*. Aerosporin and polymyxin both appear to be basic polypeptides, but they give different products on acid hydrolysis. Aerosporin yields the amino-acids leucine, threonine, and *xy*-diaminobutyric acid, whereas polymyxin yields serine on hydrolysis. Neither antibiotic penetrates the blood-brain barrier. The earlier trials with aerosporin showed that it contained a factor which damages the renal tubules, and this was a serious obstacle to its clinical use. More recently, however, aerosporin free from any nephrotoxic action has been isolated from a special strain of *B. aerosporus*, and clinical trials with this are in progress. Swift's preliminary report on the treatment of pertussis with aerosporin suggested that it does good if given early enough. This agreed with the report of Brownlee and Bushby that a single dose of the antibiotic protected 90 per cent of animals experimentally infected with many lethal doses of *H. pertussis*. In the treatment of pertussis aerosporin has the disadvantage that it must be administered parenterally every four hours, which is trying not only for the patient but also for the nurse or doctor.

Both polymyxin and aerosporin are still in the clinical trial stage and are not yet obtainable for general use.

Natural Reservoir of Poliomyelitis

(Reproduced from *Medical Newsletter* No. 16a-160 dated July 1949 prepared by the American Medical Association)

Four anticipated features of a natural host for poliomyelitis would be :

1. That it will be found throughout the temperate and tropical zones.
2. That it will account for the frequently observed tendency of the disease to start and to have a higher incidence in rural than in urban populations.
3. That it will account for the seasonal tendency of the disease in man.
4. That it will be so inconspicuous as to have escaped consideration to date.

After considering the fossorial habits and the geographic distribution of the ground mole, the possibility of this animal fulfilling the four anticipated features of a natural host for poliomyelitis was discussed by Rector in a recent article. It is obvious that a higher percentage of the rural than of the urban population comes in contact with these animals; yet the prevalence of moles in the city parks offers urban dwellers sufficient contact with them disregarding trips to the country.

Furthermore, spot maps of urban epidemics of poliomyelitis frequently show a centripetal spread.

Successful passage of the virus from mole to mole and from mole to Swiss mouse and cotton rat is reported. Attempts to pass the virus to three monkeys have been unsuccessful, however. Forty-three moles have been exposed to, or inoculated with, virus of poliomyelitis obtained from the following sources: mouse brain experimentally infected with the rodent-adapted strain of Lansing virus, brain and spinal cord of a human patient who died of poliomyelitis, and stools of four infected human beings. Of these animals, but two have survived.

Two distinctly different types of terminal behaviour are described. The survival time of the infected animals is unpredictable, regardless of the source of the inoculum, the route of inoculation or the relative position of the animal in serial passage. There is not any tendency of the virus to become fixed. Possible routes of inoculation other than intracerebral have not been adequately investigated. The absence of typical histopathologic lesions of poliomyelitis in the moles and the Swiss mice and cotton rats in which passage of mole brain and spinal cord was effective is discussed, however the lack of such lesions is not unique in the mole, since the pathological condition observed in rabbits and monkeys does not duplicate that of the usual human or simian lesions.

Fifteen animals were employed as controls for comparative studies of autolytic changes, dietary deficiency, ability of the mole's brain to respond with mobilization of inflammatory cells, trauma of handling and reaction to foreign protein. Investigation is still in progress concerning such questions as to which strains of virus the mole is susceptible, by what routes of inoculation infection is possible, whether the mole flea is a vector or possible intermediary host and the possibility of eventually producing lesions.

(Rector, L. E., M.D., St. Louis, Mo.: The Mole as a Possible Reservoir of Poliomyelitis. *Archives of Pathology*, 47, 366, April 1949.)

Aureomycin Therapy in Human Brucellosis due to *Brucella melitensis*

By W. W. SPINK *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 138, 18th December, 1948, p. 1145)

AUREOMYCIN is an antibiotic which Duggar of the Lederle Laboratories obtained from the mold *Streptomyces aureofaciens*. The oral administration of aureomycin with sulphadiazine was begun in July 1948 in a group of patients with infections due to *Br. melitensis*.

The clinical results far surpassed the expectations, and it later became evident that aureomycin alone, in relatively small oral doses, altered the clinical course of the disease in a most dramatic way. Though a longer follow-up period is essential for the complete evaluation of aureomycin, a report of the experience to date with this antibiotic is warranted because of the remarkable clinical results that have been obtained.

One reaction that can be ascribed only to the drug was seen so frequently that it must be detailed. It was seen in 12 of the 24 patients about eight to twelve hours after the first oral dose of aureomycin. The patients experienced an abrupt rise in temperature over that which had been present previously. This single spike in temperature was occasionally accompanied by a shocklike picture with a drop in blood pressure and tachycardia. Although some apprehension was attached to these phenomena, no serious consequences followed. It was observed that this type of reaction occurred when a dose of 0.5 gm. was given every six hours. When smaller doses of aureomycin were administered initially, fewer of these effects were seen.

The only other side effects pertained to the gastrointestinal tract. These consisted of nausea, vomiting and mild diarrhoea. However, the manifestations were transitory and not severe enough to warrant discontinuation of therapy.

The recommended doses of aureomycin for melitensis infections are as follows: a total of 0.1 gm. given the first day in four divided doses, a total of 0.6 gm. the second day, 1.6 gm. the third day and 2 gm. the fourth day. The drug should be administered for a total of ten days. This schedule is recommended until more information is forthcoming concerning the 'Herxheimer-like' reactions and the amounts necessary to produce permanent recovery.

Aureomycin has been administered orally to 24 patients having bacteriologically proved acute and chronic brucellosis due to *Br. melitensis*. The immediate therapeutic results have surpassed those obtained with any other specific therapy, including a combination of streptomycin and sulphadiazine. The toxic reactions due to aureomycin have been mild. Unless small initial doses of the drug are used, a febrile reaction associated with a drop in blood pressure may be observed. The severity and frequency of these phenomena have been reduced with the administration of small doses of drug at the beginning of treatment. It is emphasized that these encouraging results in the therapy of human brucellosis are concerned only with the immediate effects on the clinical course. These patients are being followed closely for clinical and bacteriologic relapses, and only after a lapse of several months can a definitive statement be forthcoming.

Further bacteriologic studies have been carried out over a period of one to three months following therapy. A total of eighty-two cultures of blood from the 24 subjects have been studied. One patient (case 9) has had no symptoms but there has been slight fever and one of four cultures taken after treatment showed *Br. melitensis*. Another patient (case 15) has had fever; the spleen has been palpable, and one of four cultures yielded *Br. melitensis*. This patient had an extremely severe infection and was not expected to live before treatment was started. One patient (case 14), who is now pregnant eight months and who had no fever or symptoms of brucellosis, had one of four blood cultures positive for *Br. melitensis*.

It is possible that the use of larger doses of aureomycin will prevent bacteriologic relapses. It is now recommended that a total daily dose of 4 to 6 gm. for two weeks be used rather than 2 gm.

Diet in Ulcerative Colitis

(From the *Journal of the American Medical Association*, Vol. 138, 13th November, 1948, p. 857)

THE following dietary programme has served well. The activity of the disease will determine the phase of the diet on which a patient is placed.

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	Unit	Foundation diet	Full diet
Carbohydrates	Gm.	195	270
Protein	"	85	145
Fat	"	125	215
Calories	"	2,240	2,600
Calcium	Mg.	470	1,940
Iron	"	11	17
Vitamin A	I.U.	4,300	7,800
Thiamin	Mg.	1.4	2.5
Riboflavin	"	1.5	4.0
Nicotinic acid	"	14	18
Ascorbic acid	"	35	105

The initial or foundation diet is served to patients with chronic ulcerative colitis. At the outset of a well-ordered programme, it is a diet low in residue. Additions of food are made as tolerated so as to increase the calories and protein as quickly as possible. One additional food as well as increased size of servings is given each day unless otherwise ordered by the physician. Protein concentrates may be used or non-fat milk solids may be added to fruit juices or milk as suggested here. In general, the use of tobacco and alcohol is contra-indicated in patients with active ulcerative colitis. The question of medicinal therapy is difficult to answer because new drugs are constantly coming into use. Among the sulphonamide compounds, the most satisfactory ones have been phthalylsulphathiazole, 15 to 22½ grains (1 to 1.53 gm.) every three hours, and azosulphamide ('neoprontosil'), 10 to 15 grains (0.6 to 1 gm.) every three hours. These drugs can be given for approximately two weeks at a time for the average patient, and after a rest of a week or so they may be resumed for a similar period of two weeks. Innumerable other drugs are being used, and these will be found in current publications.

Streptomycin as an Adjunct in Treatment of Acute Pulmonary Tuberculosis

By E. R. LEVINE *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 138, 13th November, 1948, p. 808)

STREPTOMYCIN is not effective in the treatment of chronic pulmonary tuberculosis with well-established cavities. However, for this condition, as well as for acute tuberculosis with rapid caseation, cavitation and pneumonic spread, streptomycin was used as an adjunct to the regular and accepted methods of collapse therapy and excision. The authors have observed it to be the most valuable single medicament known.

To date, the disease in 19 patients, all of whom presented lesions which were impossible to treat or could be treated only with great risk, has been controlled successfully by this means. Apparently streptomycin therapy caused a decided diminution of toxic symptoms, inhibited further spread of the disease and aided in the resolution of recent infiltrations. This had the effect, in general, of altering a lesion so that it could be successfully treated by standard methods.

In pulmonary tuberculosis, with the exception of early simple exudative disease, streptomycin therapy should not be instituted until a complete plan for the treatment of the patient has been formulated. There is great danger in using streptomycin too early, in that its effectiveness may be lost by the time collapse therapy or other surgical procedure is needed, and the assistance thus rendered would be wasted.

It has been noted that in these two types of disease, streptomycin therapy, although not successful in producing a cure, had certain definite effects. There was decrease in temperature and in other toxic symptoms, and no further spread of the disease occurred while recent infiltrations became resolved. Considered in the light of collapse therapy, this means that the factors which prevent treatment or interfere with successful completion are eliminated by the use of streptomycin.

Susceptibility to Cholera

By SAID ABDOL

(Abstracted from the *Lancet*, i, 12th June, 1948, p. 903)

THE 1947 epidemic of cholera in Egypt had a very erratic distribution. Study of a particular district shows that most of the victims were either parasite-ridden people, especially when pellagra, malaria, or old age was superadded, or young children, especially convalescents from measles.

Cholera seldom attacked more than one member of the same household living under the same conditions. This is also a feature of pellagra in Egypt.

Cholera vibrios are rapidly destroyed by stomach contents of normal acidity. Persons with low gastric acidity or achlorhydria are deprived of this defence against the disease and are therefore susceptible.

Achlorhydria may be due to causes common to all countries, such as childhood, old age, starvation, infections, general diseases, heredity. In Egypt it is, in addition, commonly due to parasitic infection.

If the vibrio crosses the stomach barrier, its further fate depends on many factors, of which the intestinal pH is perhaps the one that determines the development of disease, or of the carrier state, or the destruction of the vibrios.

The Control of Infection in Burns

By L. COLEBROOK *et al.*

(Abstracted from the *Lancet*, i, 12th June, 1948, p. 893)

Most of the sepsis of burns is due to hospital infection and can be prevented if the right conditions and appropriate routine are established. The complete elimination of such infection should be the target in all treatment of burns.

Two distinctive objectives have to be kept in view: (1) blocking the transmission of pathogens to the burns at the time of the dressing; and (2) blocking their transmission to the burns between one dressing and the next while the burns are (in theory) adequately covered.

The first of these objectives has been successfully attained during the three-year period in the burns unit at the Birmingham Accident Hospital (734 cases treated) by carrying out all dressings by a trained team using a strict aseptic technique, in a room ventilated by an abundant stream of filtered air. The number of patients infected by hæmolytic streptococcus and pyocyanæa at the time of dressing under these conditions has been less than 1 per cent.

The second objective has proved much more difficult, and the success achieved has been less complete. The great majority of the infections transmitted in the wards between one dressing and the next occurred in patients whose burns were difficult (or impossible) to cover adequately with dressings—e.g. burns of the buttocks and perineum or the face—or in patients who interfered with their dressings, conveying pathogens directly to the wounds or allowing contaminated dust particles to reach them. When dressings become

soaked with serous exudate during the first few days after burning, pathogens conveyed to the outer bandages from the air or from bedding are able to 'grow through' the dressing and so infect the burned surfaces. The use of cellophane as a bacterial barrier to prevent this is suggested.

Streptococcal infections have proved the easiest to control, because they can be quickly eliminated from the burns by local application of penicillin (or of sulphonamides), thus reducing the reservoir of potentially infective cases to a low level. Infection by pyocyanea and staphylococcus, which could not be eliminated so quickly or so certainly from the wounds, were much more difficult to control.

In view of the manifold opportunities for cross-infections presented by a large ward full of burned patients, and the highly infectible nature of the wounds, it is concluded that the best way to maintain a high level of freedom from hospital infection would be to nurse all burns during the first few weeks in single-bedded well-ventilated cubicles, each of which could be readily fumigated after it had housed any infected case. Strict barrier nursing of infected cases would also be necessary.

Intravenous Iron

(From the *British Medical Journal*, i, 22nd January, 1949, p. 163)

INTRAMUSCULAR injections of iron are not widely used in Britain, as an adequate amount cannot be given without risk of toxic symptoms and the injections tend to be painful. Nissim (*Lancet*, 1947, 2, 49) reported the use of intravenous saccharated iron oxide. The commercial preparation 'ferrivenin' is now available for the treatment of hypochromic anæmias which prove refractory to oral therapy. Each 5-ml. ampoule contains 100 mg. of elemental iron as an iron-sucrose preparation, and it is claimed that there is '100 per cent utilization' of such iron as compared with about 14 per cent for ferrous sulphate and 1.5-3.0 per cent for ferri et ammon. cit. taken by mouth. A test dose of 1.5 ml. is injected intravenously on the first day, 3 ml. on the second, and subsequently 5 ml. or 10 ml. either daily or on alternate days until a 'satisfactory response' is obtained. Intravenous injections should be carefully performed, and it is important to prevent any of the iron solution escaping into the tissues. Reactions—for example, malaise, pain in the back, etc.—may occur, but are uncommon. When injections are given slowly (about 2 ml. a minute), venous thrombosis does not often take place and no 'washing through' of the needle with glucose saline is necessary. As 25 mg. of iron are calculated to raise the hæmoglobin 1 per cent, it is reckoned that each ampoule should increase the hæmoglobin by about 4 per cent. A large infusion of 5 per cent glucose with 2 per cent ferrivenin has been suggested in order to avoid repeated venepuncture. Further reports of the latter technique are awaited. In the case mentioned, intravenous iron would seem well worthy of trial. In every case of so-called refractory iron-deficiency anæmia, however, it is all-important to make sure that the anæmia is not secondary to such conditions as reticulosis, neoplasm, or nephritis, and that there is no evidence of blood loss.

Electrical Reactions of Muscle in Poliomyelitis

By IAN G. MACKENZIE, M.D.

(Abstracted from the *Proceedings of the Royal Society of Medicine*, Vol. 42, No. 7, July 1949, p. 488)

THERE is one fundamental difference which enables a distinction to be made between the curves of a muscle that will recover and those of a muscle that will not.

In a muscle that is going to recover the curves remain essentially normal in shape, in the early stages of the disease, even though their position may alter; that is to say even though higher voltages than normal are required to elicit a response. In a muscle that will not recover, the shape of the curve is abnormal, although the threshold voltages at long durations of stimulus may be even lower than normal.

The optimum time for making this distinction, that on which the prognosis is based, is probably the fourth week after the onset of the disease. By then the changes in the anterior horn cells are said to be maximal, and it is then still relatively easy to differentiate the two types of curve.

The practical application of these results is obvious. If the prognosis is good, one can contentedly spend long periods of treatment on rest and re-education. If the prognosis is bad, one should proceed at an early date to order any necessary supporting apparatus for the patients, and get them up, thereby saving weary months during which they do little but learn the names of muscles that they will never use.

This is a mere sketch of the subject of electrical reactions in poliomyelitis, and it is given in this incomplete form only because it is believed that some of these patients can be saved unnecessary months of immobilization, and in the hope that others will interest themselves in the problem and prove or disprove the thesis.

Reviews

GAS AND AIR ANALGESIA.—By R. J. Minnett, M.D., D.A. Third Edition. 1947. Baillière, Tindall and Cox, London. Pp. vii plus 80. 18 illustrations. Price, 5s.

THIS small publication deals with the development and the technique of gas-air analgesia apparatus and the technique of induction of analgesia in women during labour in order to avoid excruciating pain during parturition.

The use of gas and air analgesia for the relief of pain is one of the outstanding events that have taken place in the present generation. The author has made an effort in the book to bring forward the technique in simple words before the practitioners and the midwives and has discussed various modifications of the original apparatus with photographs and the contra-indications in the gas anæsthesia to minimize the danger and to give relief to the expectant mother from anxiety and suffering which the childbirth entails.

The air-gas analgesia may be introduced by the patient herself if trained beforehand. The book is recommended to the obstetricians, midwives and the anæsthetists attached to maternity hospitals.

J. S. C.

GAS AND AIR ANALGESIA.—By R. J. Minnett, M.D. (L'pool), D.A. (R.C.P. and S. Eng.), F.F.A., R.C.S. Fourth Edition. 1949. Baillière, Tindall and Cox, London. Pp. 88. Illustrated. Price, 5s.

THIS edition had to be prepared as there was a great demand for the book. In addition to the full description of the various gas-air analgesia apparatus now in the market and the details of the induction of analgesia, the author has added another chapter (chapter III) which gives technique of the administration of analgesia, specially for the use in midwifery. This edition, therefore, will be more useful for midwives and is particularly recommended to them for study.

J. S. C.

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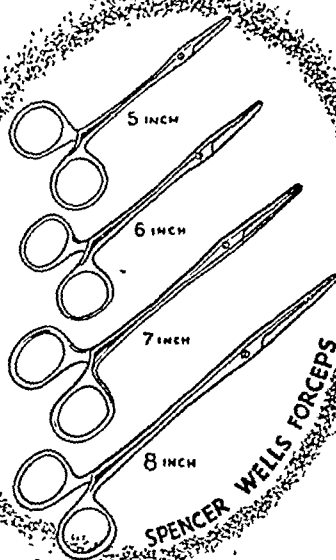
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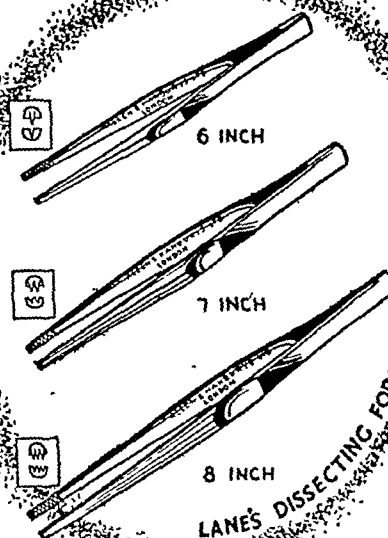
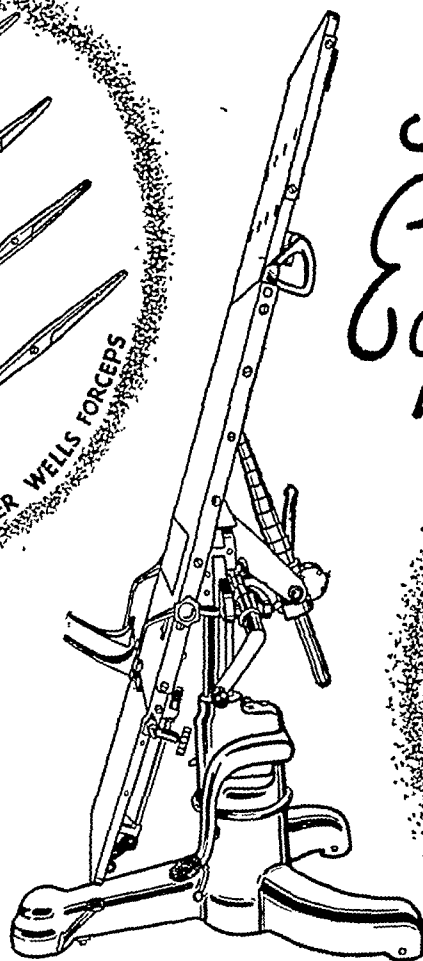
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AIDS TO ANÆSTHESIA.—By Victor Goldman, L.R.C.P., M.R.C.S., D.A. (R.C.P. & S.). Second Edition. 1948. Baillière, Tindall and Cox, London. Pp. vii plus 316. Illustrated. Price, 7s. 6d.

THE introduction of the book starts with the words 'No anæsthetic agent is safer than the person who employs it'. The statement is perfectly true since safety of an anæsthetic depends a good deal on the knowledge and experience of the anæsthetist himself. It is the duty of the anæsthetist to select the proper type of anæsthetic, and to maintain life during the period of a surgical operation by preventing the pain shock and to keep up the heart and the respiratory system properly functioning.

This handy book has condensed the main and essential information regarding different types of anæsthetics, their application in different pathological and surgical conditions. The book consists of 23 chapters with an appendix full of useful informations. The chapters deal with physiology and pharmacology of anæsthetics, different stages of anæsthesia and the administration of anæsthetics by various routes as by inhalation, infiltration, intravenous, intrathecal, and dental, etc. Two chapters have been devoted to the history of anæsthetics and the biography of workers who played an important rôle in the discovery of anæsthetics. In the present edition certain chapters have been rewritten to incorporate the knowledge and experience gained by the author during the World War II.

The book is recommended as a useful aid to the medical students, house surgeons and the post-graduates.
J. S. C.

BONE MARROW BIOPSY.—By S. J. Leitner. English Translation by C. J. C. Britton and E. Neumark. 1949. J. and A. Churchill Limited, London. Pp. xi plus 433. Illustrated with 7 plates (6 in colour) and 194 text-figures. Price, 42s.

INDISPENSABLE to workers on hæmatology, this English translation of Leitner's famous book is intended for clinical work. Although the main emphasis, here, is on the effect of various diseases on any particular bone marrow cell or on the marrow pattern as a whole, the book, nevertheless, discusses hæmatological problems in a general way. Leitner's treatment of these problems is a mature and practical approach in which the results of the sternal marrow biopsy are integrated with other clinical and laboratory findings. Scattered throughout the text are a number of illustrative cases with short histories, in support of the points made by the author, a summary of which appears at the end of each section.

In this English edition, an attempt has been made by Dr. C. J. C. Britton and Dr. E. Neumark, the revisers, to include important American and English works not contained in the German edition and this would naturally make the volume more welcome to English-speaking readers.

An important feature of this valuable text is a series of illustrations, mostly photomicrographs, which greatly enhance its usefulness.

D. N. M.

THE MEDICAL ANNUAL: A YEAR BOOK OF TREATMENT AND PRACTITIONER'S INDEX.—Edited by Sir Henry Tidy, K.B.E., M.A., M.D. (Oxon.), F.R.C.P., and A. Rendle Short, M.D., B.S., B.Sc., F.R.C.S. Sixty-sixth Year. 1948. John Wright and Sons Limited, Bristol. Pp. lxxvi plus 414. Illustrated. Price, 25s. (Subscription price, 22s. 6d.)

This year book of treatment, now in its sixty-sixth year, contains notable advances in medicine, surgery, obstetrics, gynaecology and allied subjects summarized by a body of distinguished authors. The editors, Sir Henry Tidy and Professor A. Rendle Short, review in their introduction some topics of special interest. As usual, there is the practitioner's index giving short

descriptions of recent pharmaceutical products and medical and surgical appliances, etc. This is a book for both specialists and general practitioners.

R. N. C.

A SYNOPSIS OF PHYSIOLOGY.—By A. Rendle Short, B.Sc., M.D., F.R.C.S., C. L. G. Pratt, O.B.E., M.A., M.D., M.Sc., and C. C. N. Vass, M.Sc., Ph.D., M.B., Ch.B. Fourth Edition. 1948. John Wright and Sons, Limited, Bristol. Pp. 346. Illustrated with coloured and other diagrams. Price, 20s.

THE fourth edition of this book has appeared after an interval of ten years, necessitating a complete revision. For this Professor Rendle Short has enlisted the help of Dr. C. L. G. Pratt and Dr. C. C. N. Vass. It presents a fairly full summary of modern physiology and should be very useful to students for quick revision and also to practitioners who wish to refresh their knowledge in this subject.

R. N. C.

MATERIA MEDICA, PHARMACY, PHARMACOLOGY AND THERAPEUTICS.—By William Hale-White, K.B.E., M.D. (Lond.), M.D. (Dub.), LL.D. (Edin.). Twenty-eighth Edition. Revised by A. H. Douthwaite, M.D., F.R.C.P. (Lond.). 1949. J. and A. Churchill Limited, London. Pp. viii plus 532. Price, 16s.

HALE-WHITE'S *Materia Medica* needs no introduction. Since 1892 when the book first appeared it has served many generations of students successfully and, we are confident, it will serve many more. The present edition has been revised, incorporating the changes in the new British Pharmacopœia of 1948. The easy style and practical character of the book have been maintained.

R. N. C.

PHYSICIAN'S HANDBOOK.—By John Warkentin, Ph.D., M.D., and Jack D. Lange, M.S., M.D. Fourth Edition. 1946. University Medical Publishers, Chicago, Ill. Pp. 282. Price, \$1.50

THE fourth edition of the 'Physician's Handbook' by John Warkentin and Jack D. Lange deserves praise. It contains a good deal of material condensed in the form of a pocket reference book. The diagnostic procedures and factual data which a physician may desire to have quickly available are summarized in this book. A practitioner who slips it into his pocket or bag would find it very helpful.

R. N. C.

PRACTICE OF MEDICINE. PARTS III AND IV. WRITTEN IN BENGALI. VOLUME II.—By Dr. Jotindra Nath Ghosal, L.M.S. Published by Mr. B. Ghosal, 83, Karbala Tank Lane, Calcutta 6. Pp. 354. Price, Rs. 10

THIS volume includes the third and fourth parts of Dr. Ghosal's 'Practice of Medicine' written in Bengali. References to the author's personal observations are plentiful. The format is good and price reasonable.

R. N. C.

SHISHU-O-STREE CHIKITSA (TREATMENT OF FEMALE AND CHILDREN DISEASES). WRITTEN IN BENGALI.—By Dr. Jotindra Nath Ghosal, L.M.S. 1356 B.S. 1949. Published by Mr. B. Ghosal, 83, Karbala Tank Lane, Calcutta 6. Pp. 171. Price, Rs. 8

THIS book, written in Bengali, deals with the management of maternity cases and treatment of diseases of children. Village practitioners will find it useful.

R. N. C.

OBSTETRICS AND GYNÆCOLOGY (A SYNOPSIS GUIDE TO TREATMENT).—By B. M. Willmott Dobble, M.A., M.B., F.R.C.S., D.M.R.E. 1948. Published by H. K. Lewis and Co., Ltd., London. Price, 20s.

THIS is a book the like of which we have not had the pleasure of studying in recent years.

The author says in the preface 'It is to the general practitioner, above all, that these pages are addressed'. We also think that he alone is the person who is likely to be benefited. As mentioned by the author, the book deals almost exclusively with treatment and lays a much-needed emphasis on preventive treatment.

In the section on Labour, two separate chapters deal with domiciliary midwifery, one on normal labour and the other on abnormal labour. This is a departure from the routine practice. Its usefulness is, however, questionable, in this part of the world, midwifery both normal and abnormal is wholly domiciliary and what is strictly normal is practically rare.

The gynaecological part has necessarily been less elaborately dealt with. That is the intention of the author as mentioned in the preface. Whatever little has been written will only excite the curiosity of the reader and very often leads him nowhere. This is illustrated in the chapter on 'Prolapse and allied conditions' where some of the operations, to be performed only by the specialists, have been casually described. 'Endometriosis' is not a subject for the general practitioner to deal with. On page 301 it is written 'Chorionepithelioma—hysterectomy with oophorectomy should be followed promptly by x-ray therapy'. The inquisitive practitioner may ask, what is to be done with the tubes? Is the hysterectomy total or sub-total? What is meant by promptly, a week or a month after the operation? It is not safe to write too little, just as it is of no use to write too much.

If the author's intention is to deal with treatment alone, we cannot understand the significance of—'Having wiped its face, she should at once show it to the mother'—an exhortation by the author in italics on page 76. It is demanded (again in italics), the mouth should be cleansed before the eyes are swabbed. We think the danger of infection to the eyes is more serious. We shudder to think of the consequences of pulling the cord and placenta by the hand that is best utilized in controlling the fundus (*vide* page 107). We have yet to appreciate the ease with which the occiput is rotated and delivered with forceps after it has taken the short posterior rotation by the author as mentioned on page 136. Says the author on page 146 'They (the legs) are almost always extended in primiparae'. We respectfully beg to differ.

The get-up and the printing of the book are of a high order. It is highly appreciated that the author has stated in the preface that it is not a textbook. It would be safe in the hands of practitioners who may discriminate between what is good and which is otherwise in the subject-matter. Because of so much matter which is entirely individualistic, the book will have a limited appreciation.

M. N. S.

PRINCIPLES AND PRACTICE OF OPHTHALMIC SURGERY.—By Edmund B. Spaeth, M.D. Fourth Edition. 1948. Henry Kimpton, London. Pp. 1044 with 649 illustrations containing 1,251 figures and 8 coloured plates. Price, 75s.

THIS well-known and standard book on the surgery of the eye is a mine of information and of immense use. The new edition contains much new material and additional illustrations. The recent experiences in dealing with battle casualties have been added to the section on traumatic conditions. The sections on muscles have been expanded, especially in paralytic strabismus. The section on Plastic Surgery continues to be one of the best parts of the book. The high standard of printing and paper is maintained. The new edition will be very welcome.

E. J. S.

REFRACTION OF THE EYE.—By Alfred Cowan, M.D. Third Edition. 1948. Henry Kimpton, London. Pp. 287 with 187 illustrations and 3 coloured plates. Price, 27s. 6d.

THIS book on the theoretical and practical aspects of the refraction of the eye is suitable for the D.O.M.S.,

student. Theoretical aspects are dealt with in considerable detail, though some of the paragraphs are perhaps rather too condensed and could be more clearly expressed. The practical application of the prescribing of spectacles is well done and there is much clinical information.

E. J. S.

PRACTICAL ORTHOPTICS IN THE TREATMENT OF SQUINT AND OTHER ANOMALIES OF BINOCULAR VISION.—By T. Keith Lyle, M.A., M.D., M.Chir. (Cantab.), M.R.C.P. (Lond.), F.R.C.S. (Eng.), and Sylvia Jackson, S.R.N., D.B.O. Third Edition. 1949. H. K. Lewis and Co., Ltd., London. Pp. 271 and xii with 151 illustrations including 3 coloured plates. Price, 35s.

THE reviewer regards this book as the standard work on the subject and recommends it very highly. The chapter on Heterophoria has been rewritten in the light of experience gained in the Royal Air Force during the recent war. Much has been added to the chapter on acquired paralytic strabismus. The description on ocular torticollis is as good as may be found anywhere. It is a splendid book, clearly written and beautifully produced.

E. J. S.

CLINICAL ENDOCRINOLOGY: FOR PRACTITIONERS AND STUDENTS.—By L. Martin, M.D. (Cambridge), F.R.C.P. (Lond.), and Martin Hynes, M.D. (Camb.), M.R.C.P. (Lond.). 1948. J. and A. Churchill Limited, London. Pp. viii plus 222 with 8 plates and 22 text-figures. Price, 15s.

ENDOCRINOLOGY is a fascinating branch of medicine, though it has many difficulties. Our knowledge is still far from perfect, and the application of that knowledge has not been made easy by the complexity of the subject and over-enthusiasm of the pioneers. New advances are being made, but the general practitioner has neither the time nor the opportunity to follow them. This book is therefore to be welcomed as presenting a difficult subject in a readable form and within a small compass. It deals mainly with the following subjects: pituitary, pineal body, thyroid, parathyroid and adrenal glands, thymus, testes and ovary; their functions and the diseases arising from their disorders. The subject has been dealt with from the viewpoint of the general physician. The clinical syndromes are described with their physiological and pathological background, and the uses and limitations of hormone therapy are clearly indicated.

R. N. C.

GENERAL ENDOCRINOLOGY.—By C. J. Donnell Turner, Ph.D. Published by W. B. Saunders Company, London and Philadelphia. Pp. 604. Price, 35s.

ENDOCRINOLOGY is a subject which has been making gradual advance for some time past. Recently however the advance has been made with such a speed and the data accumulated therefrom have brought to light with such bewildering rapidity that increasing difficulty is being felt to properly evaluate some of the conflicting evidence which had gathered round the subject.

We therefore welcome the book, because it appears to us that the author has presented the subject-matter in an excellent way and has described the practical and experimental methods very clearly. The essential theoretical considerations have also been well described without giving embarrassing amounts of details.

The book can in no sense be considered as a clinical treatise. The author has approached the subject-matter from a more or less experimental rather than clinical point of view and particular attention has been directed to the operation of the co-ordinatory mechanism in plants, invertebrates and vertebrates. We are inclined to agree with the author when he describes the hormone as chemical co-ordinators and in his opinion the term should not be restricted to the products of circumscribed ductless glands only but should be widened

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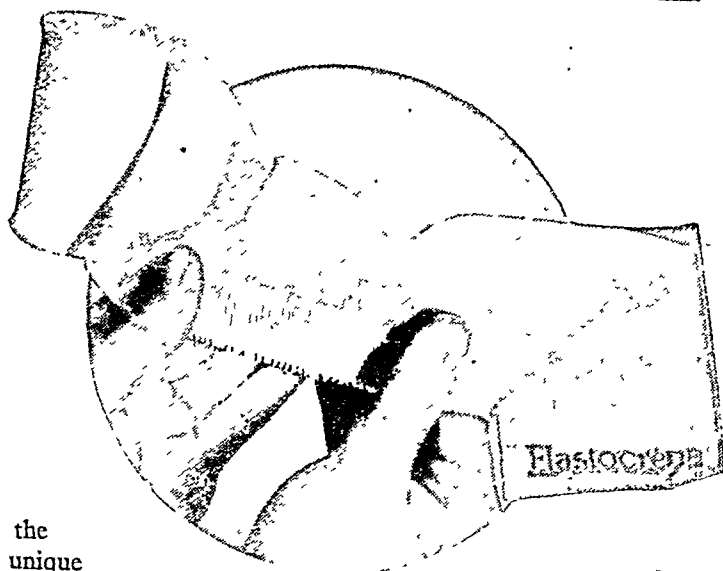
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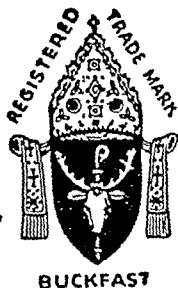
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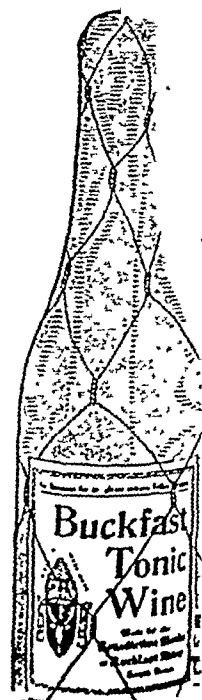
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to include similar co-ordinatory agents liberated by localized groups of cells, which do not have a sufficient degree of morphological differentiation to be admitted to the conventional category of 'ductless glands'.

The author's approach to the subject-matter is quite systematic and he has presented the subject as a fundamental aspect of biological science rather than a medical speciality. This way of approach in our opinion will be appreciated by most beginners.

We recommend the book to all those who are interested in the subject of general endocrinology.

J. P. B.

A DIABETIC MANUAL FOR THE DOCTOR AND PATIENT.—By Elliott P. Joslin, M.D., Sc.D. Eighth Edition. 1948. Henry Kimpton, London. Pp. 280. Illustrated. Price, 12s. 6d.

We welcome the eighth edition of this popular book of Professor Joslin, written mainly from the point of view of educating diabetic patients. The book is full of informations which would be of use not only to laymen but also to the junior members of the profession who will get substantial help from it to advise their diabetic patients.

The book deals, in a short space, with almost all the aspects of diabetic life, so that if the information given in the book is followed by the patients, they can live the normal span of life with comfort. Chapter IV dealing with questions which the diabetic patients are likely to ask their doctors have been answered in a clear and lucid style. Chapter VIII dealing with hygiene for the diabetics will also prove to be very valuable as it gives clear instructions as to what the diabetics should or should not do. We have no doubt that the book will prove to be as popular as its predecessors.

J. P. B.

A.M.A. (AMERICAN MEDICAL ASSOCIATION) INTERNS MANUAL. 1948.—Published by W. B. Saunders Company, Philadelphia and London. Pp. 201. Price, 12s.

This has been compiled by the American Medical Association, and though primarily meant for hospital interns in that country, it contains a lot of essential information often required in daily practice. The nature of the subjects treated will be apparent from the following main chapters: 1. Clinical and laboratory data (treatment of common emergencies, examination of blood, urine and spinal fluid, gastric analysis, etc.). 2. Drug administration. 3. Materia Medica—useful drugs arranged alphabetically. 4. Acute poisoning (diagnosis and treatment). 5. Diet and nutrition (adequate diet, special diets, etc.). The book gives useful basic data which can be quickly referred to, and it slips into the pocket.

R. N. C.

BOOKS RECEIVED

1. Chikitsa-Jagat. Vol. XX, No. 8, June 1949. A monthly medical journal written in Bengali. Edited and published by Dr. Amulyadhan Mukharji from 27C, Upper Circular Road, Calcutta. Annual subscription Rs. 4. Price per copy annas 6.

2. Serologische Reaktionen und Immunität bei Malaria. von Dr. Med. Hartwig Hormann. Band 5. 107 S., 42, Kurven-Abb., Kart. DM 7. 50. Published by Hippokrates-Verlag Marquardt & Cie., Stuttgart-S.

3. Immunity Bulletin, May 1947 to April 1948. Published by the Bengal Immunity Research Institute, 39, Lower Circular Road, Calcutta 16.

4. International Health Bulletin of the League of Red Cross Societies, Geneva. Vol. I, January-March 1949, No. 1. A review issued every three months, in French and English, by the League of Red Cross Societies, Health Bureau. Edited by Dr. G. Alsted and

Dr. Z. S. Hantchev. Address:—League of Red Cross Societies, 8, Rue Munier-Romilly, Geneva, Switzerland.

5. Chikitsa-Jagat. Vol. XX, No. 9, July 1949. A monthly medical journal written in Bengali. Edited and published by Dr. Amulyadhan Mukharji from 27C, Upper Circular Road, Calcutta. Annual subscription Rs. 4. Price per copy annas 6.

6. Proceedings of the Second All-India Compost Conference and Second Meeting of the Central Manure (Compost) Development Committee held at Jaipur on the 16th and 17th December, 1948. Printed by the Government of India Press, Calcutta, India, 1949.

7. Compost Bulletin. Vol. I, No. 4, December 1948. Issued by the Compost Development Officer, Ministry of Agriculture, Government of India, New Delhi. Printed in India by the Manager, Government of India Press, Simla, 1949.

8. Compost Bulletin. Vol. II, No. 1, March 1949. Issued by the Compost Development Officer, Ministry of Agriculture, Government of India Press, Simla, 1949.

Abstracts from Reports

TENTH ANNUAL REPORT OF THE TUBERCULOSIS ASSOCIATION OF INDIA FOR THE YEAR 1948. PUBLISHED BY THE TUBERCULOSIS ASSOCIATION OF INDIA, NEW DELHI

THE Association entered on the tenth year of its activities in 1948 and, during that year, it had to contend with certain special problems. The after-effects of the communal disturbances and of the large scale exchange of population between India and Pakistan continued to be felt during the year. The displaced persons were concentrated in camps and the conditions of life in them were far from satisfactory. There were considerable overcrowding, insanitation and limitation of the comforts of life and these helped to increase the incidence of tuberculosis. While the magnitude of the problem is so great that action on comprehensive lines for a comparatively long period will be necessary before adequate control of the disease can be established, it is gratifying to note that the Government of India has been alive to the importance of this problem and that it has, within the limits of its resources, sought to carry out an anti-tuberculosis campaign. In this connection certain measures may be mentioned. In collaboration with the World Health Organization and the International Children's Emergency Fund, the Government of India has introduced a comprehensive programme of BCG vaccination. Arrangements have been made for the manufacture of the vaccine at the King Institute, Guindy, and it is now being prepared on a scale adequate to meet India's requirements. The vaccination programme was first started at Madanapalle in the province of Madras with the active co-operation of the Union Mission Tuberculosis Sanatorium and has since been extended to the cities of Madras, Delhi, Bombay, Baroda, Amritsar, and Calcutta. The Governments of the provinces concerned are taking an active part in the vaccination programme. The two international organizations mentioned above have also offered a number of fellowships for the training of Indians overseas in tuberculosis work.

Another important event to which attention should be drawn was the Conference of Health Ministers of the different provinces which met under the Chairmanship of the Health Minister of the Government of India in August 1948, in New Delhi. Among the subjects discussed at the Conference was tuberculosis and, in recognition of its importance, adequate attention was paid to the problem of developing anti-tuberculosis measures in India on a broad basis. The recommenda-

tions of the Conference included special measures for adoption by individual provinces in the light of existing conditions in those provinces as well as the formulation of a programme of teaching and research. The part that non-official bodies can play in providing comforts to the sick, assistance in domiciliary treatment and the provision of after-care to patients after discharge from hospital was stressed.

It is also understood that the Central Government are considering the question of making special provision for tuberculosis patients from among displaced persons.

During the year two post-graduate refresher courses were held under the auspices of the Tuberculosis Association of India. The Bombay Provincial Tuberculosis Association organized such a course of three weeks' duration in February 1948. This was attended by fifteen doctors. The next course, organized by the Mysore Tuberculosis Association in July 1948, was attended by twenty-three doctors.

Under the Government of India scheme for scholarships and short travel fellowships, Dr. B. K. Sikand, Medical Superintendent of the New Delhi Tuberculosis Clinic, was awarded a travel fellowship.

Under the scheme sponsored by the Tuberculosis Association of India for the training of doctors in the Kasauli Sanatorium and the New Delhi Tuberculosis Clinic, seven doctors took their training in the course of the year. Four of these doctors were deputed by the Government of C. P. and three by the Government of Cochin. These courses of instruction provide for practical training for nine months.

The 1948 course of training for tuberculosis health visitors under the auspices of the Association commenced in January in the New Delhi Tuberculosis Clinic. Of a total of 27 candidates who were selected, only six joined the class, two of them being women. The classes are held in Delhi for six months and in the Kasauli Sanatorium for two months. All the six candidates passed the prescribed tests and have been awarded the requisite certificates by the Association. Mrs. Saraswati Bai Gadgil of Bombay and Mr. Gurbachan Singh of Patiala stood first and second in the examination and they were awarded silver and bronze medals respectively by the Tuberculosis Association of India.

THE SIXTH TUBERCULOSIS WORKERS' CONFERENCE

The Sixth Conference of tuberculosis workers was held in Calcutta from 20th to the 23rd December, 1948. Over 130 delegates attended the Conference. The Hon'ble Dr. B. C. Roy, the Premier of West Bengal, opened the Conference. In the course of his address, Dr. Roy stressed the need for education, organization and propaganda in anti-tuberculosis work and pointed out that non-official bodies must take part in the work as well as offer constructive suggestions to governments.

It may be mentioned that this was the second conference held during the year; the first one was held in January 1948 in Madras.

AFFILIATED ASSOCIATIONS

On the 15th of August, 1947, the Tuberculosis Association of India had on it 33 affiliated associations. Of these, 21 were State associations and 12 provincial. The tuberculosis associations of Bahawalpur, N.W.F.P. and Sind have now stated that they do not wish to continue their affiliation with the Tuberculosis Association of India. During the year under report, the re-grouping of some of the States affiliated to the Indian Union so as to form larger administrative units and the merging of some others into the adjoining provinces have had their repercussion on the tuberculosis associations which existed in those States. Consequently, the tuberculosis associations of Bikaner, Jodhpur and Udaipur have joined together to form an association for Rajasthan Union with its headquarters at Udaipur. The associations of Gwalior and Holkar have joined to form the Madhya Bharat

Union Tuberculosis Association functioning at the Union Capital, Gwalior. The States of Jambhoda, Jawahar, Santrampur, Lunawada and Chota-Udaipur have merged with the Bombay province and Baroda will join Bombay in May this year. Presumably the tuberculosis associations of the States which merge into the province of Bombay will become associated with the Provincial Tuberculosis Association.

The East Punjab Association has now been formed. At its request the Central Association gave a loan of Rs. 10,000 to the East Punjab Association to carry on its day-to-day administration, as the latter has not so far received its share of funds from the previous Provincial Tuberculosis Association of the Punjab.

The other affiliated associations carried on their normal work in a satisfactory manner. Many of them concentrated on educative propaganda in respect of anti-tuberculosis measures. The Bombay Provincial Association organized a 'symposium' by medical practitioners in order to enlist their co-operation in anti-tuberculosis work. It was decided to start a clinic in association with which organized home treatment would be started in collaboration with Bombay municipality. The Provincial Association has also been actively co-operating with the local health authority and the Provincial Government in the organization of the BCG vaccination programme.

The detailed reports from the different affiliated associations are given as an appendix to this report.

TUBERCULOSIS INSTITUTIONS

A tuberculosis hospital with 110 beds in Bombay and a tuberculosis clinic in Patiala started functioning during the year under report. The construction of a tuberculosis clinic in Rajkot was completed and it is expected to start working at an early date. The number of tuberculosis clinics in India, excluding Pakistan, is 115. There are 65 tuberculosis hospitals and sanatoria, including the Sangodh Tuberculosis Hospital with 64 beds and another at Wai with 24 beds. The number of beds in such institutions in India to-day is 5,476. In addition, there are 1,839 beds for tuberculous patients in general and isolation hospitals and 600 beds for tuberculous soldiers.

DONATIONS

A sum of Rs. 5,001 was received by Lady Mountbatten as donation from Dr. Alagappa Chettiar of Madras for the Kasauli Sanatorium. Two ex-patients of the sanatorium, Mrs. Bhagwan Das Bajaj of Calcutta and Messrs. Dan Trust Jamna Das of Gaspur (through Shri Ram Kumar Arya) donated Rs. 4,000 and Rs. 5,000 respectively for the sanatorium. The Tuberculosis Association of India expresses its grateful thanks to these donors.

The Tuberculosis Association of India as the premier institution in the country for organizing anti-tuberculosis work looks forward to increasing support from governments and the public for the consolidation of the work it has already accomplished and for a growing expansion of its activities.

THE MISSION TO LEPERS: A REPORT OF THE SEVENTY-FOURTH YEAR'S WORK IN BURMA, INDIA AND PAKISTAN, FROM SEPTEMBER 1947 TO AUGUST 1948. Pp. 48 WITH ONE MAP AND 17 ILLUSTRATIONS, ISSUED BY THE INDIAN AUXILIARY

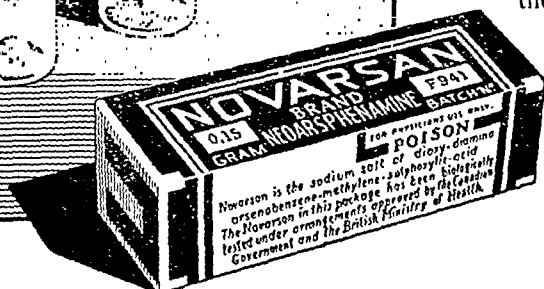
The report opens with a foreword by the Hon. Secretary in India to the Mission to Lepers, Mr. Bailey; this is followed by reports from the different leprosy homes and hospitals and homes for healthy children of leprosy patients in Burma, India and Pakistan, owned, managed or aided by the Mission to Lepers; these form the bulk of the report under review. A report from the Medical Secretary to the Mission,



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Dr. Cochrane, then follows. The last portion of the report consists of statistics of inmates and medical statistics at the end of 1947; a map showing the geographical distribution of the various institutions, together with the number of inmates in each and the name of the co-operating body where any; and finally the total expenditure and income for the Mission's work during the year 1947.

The report from individual institutions (the total number of which is 48, 31 being managed directly and 17 aided by the Mission) deals with the usual activities carried on in such places, viz, medical care, occupational therapy, including agriculture, gardening, weaving, etc., educational, social, recreational and religious ones. The Medical Secretary stresses the point that the problem of relief and rehabilitation has to be solved even if a specific cure for leprosy was found.

The total number of inmates in the Mission and aided homes was 10,070, consisting of 5,265 men, 3,045 women and 901 children patients and 859 healthy children. The total number of in-patients under treatment at the end of the year was 8,785 and the total number of out-patients treated during the year was 12,319.

The total collection from donations and subscriptions amounted to Rs. 78,151. The total expenditure for the year amounted to Rs. 17,81,724, which was mainly by contributions from the Mission to Lepers, supplemented by government and local grants.

The report reveals the quality and quantity of anti-leprosy work carried out by the Mission to Lepers in Burma, India and Pakistan. The Mission to Lepers is the pioneer worker in this field and is still the largest single body carrying on anti-leprosy activities in this part of Asia, and as such deserves support. Their devotion to duty even under adverse circumstances, the zeal and fervour with which the work is carried on, should inspire those that are engaged in or likely to be engaged in anti-leprosy activities. The report is interesting and instructive, and is nicely printed and illustrated with photographs showing different activities in some of the homes.

KING EDWARD VII MEMORIAL PASTEUR INSTITUTE AND MEDICAL RESEARCH INSTITUTE, SHILLONG. THE THIRTY-FIRST ANNUAL REPORT FOR THE YEAR ENDING 31ST DECEMBER, 1947

I.—ANTIRABIC SECTION

DURING the year a private centre was opened at Dullabcherra, Cachar, bringing the total number of antirabic treatment centres in the province to 73, of which 25 were public centres and 48 private centres. With the separation of a portion of Sylhet after the dawn of Independence, 4 public and 3 private centres in that district fell to East Bengal, Pakistan, but till the end of the year, they were kept supplied with antirabic treatments as demanded.

The total number of persons who applied for treatment during the year amounted to 3,560, of whom Shillong received 494. This shows an increase by 209 over last year's total of 3,351 and is a record figure for the Institute.

Total treated.—Treatment was completed in the case of 2,935 persons. Out of these, 95 cases treated at Sylhet have to be excluded, owing to the non-receipt of statistical cards or other information relating to them, in spite of repeated reminders. Other cases that have been excluded from the statistics consist of 296 cases that absconded without completing their treatment and 329 'advice cases', thus leaving 2,840 for statistical analysis.

Health returns.—The percentages of fully treated persons whose health cards were received six months

after completing treatment were 93.6 and 87.7 respectively for Europeans and Asiatics.

Results of treatment.—From among 2,840 fully treated persons, nine deaths from hydrophobia were reported, giving a mortality rate of 0.32 per cent. This is much higher than last year's figure of 0.14 but well below the average of 0.68 per cent for the last 31 years.

During the year, 216 prophylactic dog treatments were issued; also, post-infection treatments amounting to 71 and 39 for dogs and cattle respectively.

No health returns in respect of these animals have been received, nor was any death amongst them reported.

II.—VACCINE SECTION

The following prophylactic vaccines were issued during the year :—

1. Cholera vaccine ..	1,257,490.5 cc.
2. T.A.B. vaccine ..	55,950.5 cc.
3. Combined T.A.B. and cholera vaccine ..	3,425.0 cc.

The amount of cholera vaccine mentioned above includes 600,000 cc. supplied to the Director-General, Health Services, New Delhi, during the months of September and October 1947 and 150,000 cc. supplied earlier to Bihar.

III.—BACTERIOPHAGE SECTION

During the year, 201,496 ampoules of 2 cc. of combined cholera and dysentery bacteriophage were issued.

IV.—ENQUIRY ON NAGA SORE (INDIAN RESEARCH FUND ASSOCIATION) UNDER DR. S. R. PANDIT

The work of the enquiry has been carried out along the lines indicated in the proposal submitted.

During the period under report, ten patients with Naga sore were admitted to the Clinical Research Hospital attached to the Institute for investigation. Seven of these patients had active sores, while in the remaining three the sores were of a chronic nature. In all of them the ulcers were distributed over the lower extremities below the knee. Four cases had a single ulcer and the remaining six had multiple ulcers ranging from two to five in number. In six cases there was a history of previous trauma at the site of the ulcers. Of the remaining cases, in one it had appeared spontaneously as a bleb after initial itching, in two the ulcers had arisen from lesions due to scabies, and in the last case a leech-bite was the precursor of the ulcer. There was evidence of malaria in four patients (positive blood finding and/or enlarged spleen). Seven had helminthic infections, one had ankylostome and the rest roundworm infections. A fair number of *E. histolytica* were found in one case. In regard to Wassermann reaction, one gave a strong positive while another gave a doubtful reaction. There was no clinical evidence of malnutrition in any of the patients.

Microscopy of smears.—Dark-ground examination and smear examination of discharge were carried out from day to day in each of the cases. The fusiform organism was constantly present in each of the ulcers and there was a definite correlation between their intensity and the state of the ulcer; the more acute the ulcer the larger the number of organisms, few of them being seen when healing had proceeded far enough. Interference with healing increased their number. This corroborated the earlier findings.

In none of the cases was a *spirochæte* seen at any stage. It is, therefore, very doubtful whether this organism has any ætiological significance.

Other organisms present in ulcers were cocci, which were seen in every case, and in a few of the cases *Proteus vulgaris* and *Ps. pyocyanea*.

Reproduction of the sore.—Direct inoculation of pus from a sore by scarification or by intradermal injection reproduces the sore in the human being, but not in laboratory animals—the monkey, rabbit, guinea-pig,

white mouse and white rat are completely refractory. Even in patients of Naga sore with an active or healed ulcer, a fresh ulcer could be reproduced by this means, thus showing that immunity conferred by a previous ulcer is not of a solid nature. Out of seven cases, the sore was reproduced in six.

A thick suspension of a freshly isolated culture of *fusiformis*, injected intradermally into five human volunteers, failed to produce the sore. In four of them, there was pain and moderate induration at the site of inoculation during the first 48 hours, but it subsided subsequently. In the fifth, a purulent bleb resulted. The aspirated fluid contained no *fusiform* bacilli and healing was rapid. In a patient with healing ulcer with no *fusiform* bacilli on two or three successive days, a culture of *fusiformis* was rubbed into the ulcer but it did not flare up and no impediment to healing was observed. This experiment repeated in laboratory animals has also failed.

On the assumption that the sore might be caused by a virus alone or in association with the *fusiform* bacillus, suspensions of pus were filtered through L3 porcelain candles and the filtrates alone and mixtures of the culture and the filtrate were inoculated separately in four human volunteers by the intradermal route. The filtrates failed to produce any reaction whatsoever and no ulcer could be produced with the combination in any of the volunteers.

V.—GENERAL LABORATORY EXAMINATIONS

The number of laboratory examinations carried out during the year amounted to 10,278, which is an increase by 316 over last year's figure. The number of samples tested for the Wassermann reaction and Kahn test increased from 2,763 to 3,100.

VI.—CLINICAL RESEARCH HOSPITAL

Thirty-one persons were admitted into the hospital during the year for investigation and treatment, of which 12 were Naga sore cases, 10 kala-azar, 3 admitted for dog bite and 1 for snake bite.

ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH: ANNUAL REPORT (1948) BY THE CURATOR OF THE LABORATORY, WITH REPORT THEREON BY THE COUNCIL

THE laboratory has sustained a very great loss through the death on 11th September, 1948, of Lieut.-Colonel W. F. Harvey, who was in charge of the Histopathology Department for 20 years, during four of which he also acted as Superintendent of the whole laboratory.

During the past year, 14 workers (7 part-time and 7 whole-time) have been engaged in research in the laboratory. Two of these, Miss Bridget Cairns and Mrs. Storey, hold Carnegie Scholarships, and Dr. W. Wallace Park has a grant for whole-time research from the British Empire Cancer Campaign.

Dr. Barnard and Dr. McKail left the laboratory in November, the former to return to South Africa and the latter to take up an appointment as Lecturer on Biochemistry at Aberdeen University. Dr. T. W. Lees has replaced Dr. Barnard as Assistant Histopathologist.

The number of reports sent out from the laboratory during the year has increased by 5,305, the total number for the year reaching the record figure of 30,909. That has meant a very busy year for the technical staff.

1. RESEARCH DEPARTMENT

Histopathology

Drs. J. C. Lees, T. W. Lees and W. W. Park have continued their research on the chemotherapy of cancer, using transplantable tumours in mice. Dr. Park has

published (with Dr. R. A. Tennent of Glasgow) an article on a case of stromal endometriosis of the uterus. Drs. J. C. Lees and Park have also collaborated in an investigation into chorion epithelioma. Material from 23 cases, from this laboratory and the Gynaecology Department of the University, has been examined and commented on and a comprehensive review made of 500 cases from the literature. This work is now ready for publication.

Biochemistry

During the year 1948, research work has continued to have as its object the discovery of new chemotherapeutic agents. In the past year, the synthesis of drugs of possible antimalarial activity has been the main objective. This interest has continued, and it is noteworthy that some of the *p*-phenanthroline compounds which have been prepared have been proved to have considerable action against avian malaria.

Dr. Douglas, who holds a Medical Research Council Studentship, prepared an account of his work in the form of a thesis, for which he was awarded (in July 1948) the Degree of Ph.D. by the University of Edinburgh. Some of his work has been published in 1947, whilst another paper has been submitted to the *Journal of the Chemical Society* for publication.

Mrs. Storey, who holds a Carnegie Scholarship, began work in the laboratory in October 1947, and has studied the synthesis of derivatives of 2 : 3-benz-y-carboline and of 4' : 3'-2 : 3-quinoline. This work has made good progress, and a number of basic derivatives have been obtained which will in due course be submitted for examination in respect of their possible biological activity. In addition, a number of interesting chemical problems which were encountered have been investigated and satisfactorily elucidated.

Dr. Miller has continued his work on the examination of human milks. He has determined the chloride content and electrical conductivity of over 700 samples of human milk, and during the past twelve months a considerable proportion of his time has been taken up in the statistical analysis of his results. This he has done under the general direction of Dr. Kermack. The main result has been to confirm that mothers with an inadequate supply of milk tend to secrete milk containing an abnormally high concentration of chlorides and exhibiting an abnormally high conductivity. If during the first months of lactation the milk is of this type, the expectation of the mother being able to continue feeding her infant is significantly reduced.

Bacteriology

Dr. W. M. Levinthal has continued his work on the typing of all smooth pneumococci from the specimens sent for diagnostic purposes to this laboratory. Since this work started in January 1942, more than 1,000 strains have been identified.

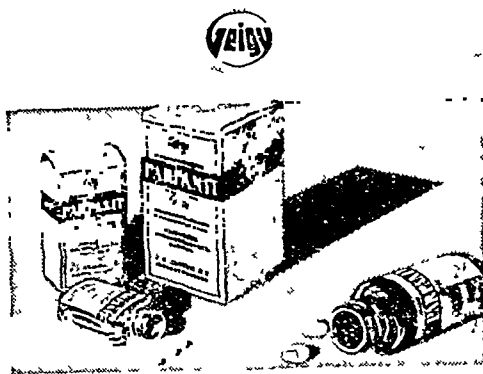
THE RAMAKRISHNA MISSION SEVASHRAM, VRINDABAN, DISTRICT MATHURA. REPORT FOR THE YEAR 1948. ISSUED BY THE SECRETARY, RAMAKRISHNA MISSION SEVASHRAM, P. O. VRINDABAN, DISTRICT MATHURA, U. P.

THE Ramakrishna Mission has been running a charitable hospital at Vrindaban since 1907.

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The total receipts during the year amounted to Rs. 66,998-1-0 and the total payments to Rs. 67,644-6-3.

Donations and subscriptions will be received by the Secretary, Ramakrishna Mission Sevashram, Vrindaban, Mathura.



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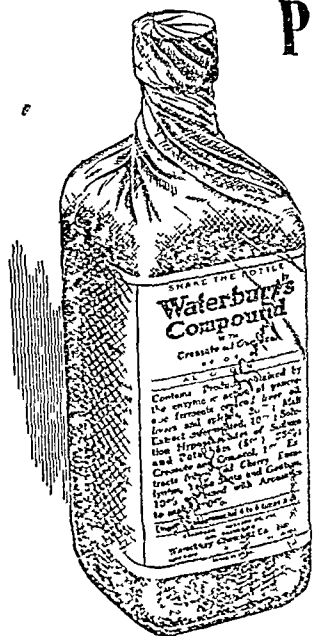
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Correspondence

STREPTOMYCIN IN TUBERCULOSIS

SIR,—Please discuss the value of streptomycin in tuberculous glands and joints.

Yours faithfully,
M. ABDULLA.

THE NURSING HOME,
VANIAKABADI.

[Please refer to the article on 'Streptomycin therapy in tuberculosis' published in the April 1949 issue of the *I.M.G.*, on page 133, and to the abstracts of interesting articles on the subject published in the 'Current Topics' section from 1948.—Editor, *I.M.G.*]

PURIFICATION OF VACCINE LYMPH BY PENICILLIN

SIR,—While Dr. Patel's results (*Indian Medical Gazette*, Vol. LXXXIII, No. 10, page 452, October 1948) are experimentally spectacular and suggest interesting possibilities, I cannot agree with his main thesis on the use of penicillin in the purification of vaccine lymph. On the contrary and without further research, the technique suggested by Dr. Patel is fraught with grave risks as the following experiments by me would indicate.

In one series of experiments, penicillin was used in concentrations varying from 500 to 2,000 units per cc. of vaccine lymph. The sterility test by the usual pourplate method, showed all the samples to be sterile within 24 hours' contact with penicillin. The potency of the vaccine lymph was also found to be unaffected. But the significant point is this. While all the samples excepting one were preserved in cold storage, one sample was deliberately kept at room temperature (Bangalore, about 23°C.). The sterility test was repeated after an interval of one month on this sample preserved at room temperature. IT WAS FOUND TO GIVE A GROWTH OF A NUMBER OF COLONIES OF STAPHYLOCOCCUS AND B. SUBTILIS GROUP OF ORGANISMS, WHILE THE SAMPLES KEPT IN THE COLD STORAGE SHOWED NO GROWTH WHATEVER. The samples were also tested for the presence of penicillin. While the samples kept in cold storage showed no appreciable loss of penicillin, the one kept at room temperature revealed almost total loss of penicillin.

These findings were further confirmed by the following experiment. Residual penicillin from the treated lymph was completely removed by alternate washing and centrifuging four times. The sediment was tested for sterility. The plate showed up a number of colonies of staphylococcus and *B. subtilis* group of organisms. But the lymph which was unwashed gave no growth whatever. It is evident that certain strains of organisms were merely inhibited by penicillin and, that when once this inhibiting penicillin is either removed or inactivated, these persisting organisms begin to show themselves up. The residual penicillin is really a mask.

It can therefore be concluded that (1) misleading results are obtained if penicillin-treated lymph samples are tested for sterility without prior and complete removal of the penicillin as the latter acts merely as an inhibitor on certain strains of organisms, and (2) penicillin could easily be removed from the vaccine lymph by repeated alternate washing and centrifuging.

In the light of these findings, I suggest that it is not prudent to use penicillin in the purification of vaccine lymph. Further research work on the application of penicillin and also of other antibiotics is called for

before evolving a technique which can be routinized with confidence.

Yours, etc.,

V. N. KRISHNAMURTHY, M.D.

VACCINE INSTITUTE,
BANGALORE CITY,
18th June, 1949.

TEACHING OF SURGERY THROUGH TELEVISION

SIR,—I would refer to the article entitled 'Teaching surgery through television', which appeared on page 204 of your May 1949 issue.

I believe that the details given in this release from the British Information Services are slightly incorrect. While I agree that Guy's Hospital in London will be the first institution in the world to have a permanent installation for televising surgical operations, I should like to mention that the Philips organization in Holland were the first in Europe to undertake this type of experiment. The occasion was the anniversary of the Leiden University in Holland where an audience of 200 medical practitioners and students in the lecture hall in one wing of the hospital watched the operation on two screens of 1.30 X 1 m. The operation was actually being performed in the operating theatre of the hospital at Leiden in a different wing of the institution.

Yours faithfully,

for PHILIPS ELECTRICAL CO. (INDIA), LTD.

R. D. RICHARDSON,

General Manager,

X-Ray and Medical Department.

Any Questions

ADMINISTRATION OF PENICILLIN

SIR,—With the increase of supply of penicillin, there has been a tendency to use it in bigger and bigger doses, sometimes 2 lacs units of sodium salt per dose up to a total of 40 or 50 lacs even in gonorrhoeal urethritis, giving 2 or 3 injections of aqueous solution daily. Is there any rationale in using such big doses and at such long intervals?

What are the doses in different infections and how should they be given?

Crystalline penicillin G(II) is being supplied with manufacturers' notes like 'refrigeration is not required, a point of great practical importance in the tropics'. It is therefore being stored and used without refrigeration by druggists and doctors alike. In an abstract from the *Pharmaceutical Journal*, Vol. 158, 4th January, 1947, page 3, published in the *Indian Medical Gazette*, April 1948, pages 197-198, it has been 'recommended that it should be stored below 77°F. (25°C.)' which however is seldom obtained in our part of the country except in winter. Will you kindly tell us if it really maintains its potency by ordinary storage in Bengal?

Yours, etc.,

N. C. DAS GUPTA, M.B.

KHULNA,

29th April, 1949.

[1. The accepted administration to-day of massive doses of aqueous solution of penicillin at 12-hourly or 24-hourly intervals is based on experimental findings. It has been found that the survival rate of experimental animals infected with streptococcus or pneumococcus depends on the total dosage of penicillin over 24 hours rather than on the extent of intervals at which it is injected; the action of penicillin continues in the body after the cessation of its circulation in the blood.

2. The dosage of penicillin necessary will vary considerably from one patient to another depending on the type and the severity of the infections. The following recommended plan of dosage will be generally useful :

Infection	Dosage
(a) Serious infections due to penicillin sensitive organisms with or without bacteraemia including bacterial endocarditis.	300,000 to 1,600,000 units (or more) per 24 hours of aqueous solution given intramuscularly or continuous intramuscular or intravenous drip. Penicillin in oil may also be used at 12- or 24-hourly interval.
(b) Chronic pyogenic infections.	300,000 units per 24 hours. Aqueous or in oil, given intramuscularly.
(c) Empyema due to penicillin sensitive organisms.	50,000 to 100,000 units once every 12 to 24 hours by injection in saline solution into the pleural cavity after aspiration of pus or fluid. Penicillin in oil should not be administered intrapleurally. The intrapleural administration may be supplemented with intramuscular injection of the penicillin in oil.
(d) Meningitis due to pneumococci, streptococci, staphylococci or sulphonamide resistant meningococci	10,000 units once or twice daily by the intrathecal route in conjunction with regular parenteral therapy (320,000 to 1,200,000) units per 24 hours.
(e) Acute gonorrhoea ..	240,000 units total.
(f) Syphilis ..	8,000,000 units in total. 1,000,000 units per 24 hours for 8 days. The administration of arsphenamine is an added precaution, specially in secondary and tertiary forms.

3. Crystalline penicillin, if kept in sealed ampoules and protected from the action of moist air, is stable at ordinary temperature. This will certainly maintain its full potency by ordinary storage in Bengal for at least two years.

B. M.]

Service Notes

APPOINTMENTS AND TRANSFERS

THE King has been graciously pleased to sanction the following promotions in, and appointments to, the Venerable Order of the Hospital of St. John of Jerusalem as Associate Officers (Brothers):—

Lieutenant-Colonel A. S. Garewal.

Lieutenant-Colonel B. S. Nat.

In supersession of the Ministry's Notification, Dr. H. P. Mehta, lately Medical Librarian in the Directorate-General of Health Services, was granted earned leave for 32 days with effect from the 25th May, 1949. On the expiry of the leave, his services were placed at the disposal of the Chief Commissioner, Himachal Pradesh.

Dr. A. B. Roy Chowdhury, Second Assistant to the Serologist and Chemical Examiner to the Government of India, Calcutta, is placed on deputation to the United Kingdom with effect from the afternoon of the 18th May, 1949.

RELINQUISHMENTS

Dr. Jivraj N. Mehta relinquished his appointment as Adviser, Ministry of Health, with effect from the forenoon of the 26th July, 1949.

The undermentioned I.M.S./I.A.M.C. officers were released from the army service on the dates shown against their names and were granted honorary ranks, as shown in the brackets against their names:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captain Das, Har Bhagwan. Dated 21st May, 1946 (Captain).

Captain Desai, Pandurao Motilal. Dated 27th May, 1946 (Captain).

Captain Doraswamy, Lakshmipuram Sreenivasiengar. Dated 27th October, 1946 (Captain).

Captain DeSouza, Anthony Theodore. Dated 17th November, 1946 (Captain).

Captain Dhurjaty, Ramachandra Rao. Dated 11th February, 1947 (Captain).

The undermentioned officer is permitted to relinquish his commission on release from the army service and is granted the honorary rank of Major:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Major Suba Singh Sidhu. Dated 23rd January, 1947.

RETIREMENT

The following officer of the late Indian Medical Service (Civil) has been permitted to retire with effect from the date shown against his name:—

Lieutenant-Colonel D. P. Bhargava. Dated 9th January, 1949.

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Original Articles

RELAPSING FEVER—TICK-BORNE

ACCOUNT OF AN OUTBREAK IN J. & K. FORCE, INDIA

By S. KAUL

LIEUTENANT-COLONEL, I.A.M.C.

Military Hospital, Madras

1. Introduction

ABOUT the middle of January 1948, a message was received from one of our forward Field Medical Units in the Jammu sector of J. & K. Force reporting the occurrence of a 'peculiar type of fever with repeated attacks accompanied by a rash over the face and feet following within a few days of being bitten by some insects' and occurring amongst some of our men occupying the forward positions cleared of the raiders. At first it was decided to send a team to investigate the condition on the spot; but owing to the extraordinary conditions prevailing at the time it was considered desirable to evacuate the cases and conduct the investigations at the rear.

The possibility of relapsing fever was immediately considered; but the 'rash' could not fit in with the usual known type of the disease as it occurred in India.

From the enquiries made from the local civil and military medical practitioners in Jammu who had worked in the locality before, the tick-borne type did not appear to be known in these areas, nor could any reference to the tick type in India be obtained from the meagre literature available.

When the patients arrived, there was no doubt left clinically that they were cases of relapsing fever of the tick-borne type. The diagnosis was confirmed, in a few days, by finding the parasites in the blood films from the cases.

Between February and June 1948, one hundred and four cases were evacuated to Jammu from forward areas in Jammu province and 4 cases from Kashmir valley, bringing the total up to 108. Of these cases 50 remained smear negative in spite of the most persistent efforts. All these smear negative cases were however clinically typical. The remaining 58 cases were, at one time or other, smear positive. Of the 58 cases, 52 had indisputable evidence of having been bitten by insects later identified as ticks. In the analysis that follows, the 52 cases which were smear positive and had evidence of tick-bites alone are included. The 50 smear negative cases and the 6 cases where the vector was in doubt have not been included.

Many difficulties, both administrative and technical, made it impossible to conduct any systematic investigations, but as this, to my knowledge, is the first recorded series of the tick-borne type of disease in India, the results, whatever they are worth, deserve recording.

2. Source

The stories told by these cases were informative and have an important bearing on one of the characteristics of this type of the disease. At one place 13 men from a platoon of a unit slept for a night in a tent pitched at the site of an old dismantled hut, some of the walls of which were still standing. At night all of them were bitten by insects described by the men as 'chichad' and later identified as ticks. This unit moved to the rear and within 10 days the bitten men went down with fever, 6 of them being admitted to the hospital within 3 days of each other and from 6 to 15 days after being bitten. None of the associates of these men who slept in other shelters or tents only 20 to 40 feet away were bitten or developed the disease. This site was again occupied by a platoon of another unit which relieved them. During the two nights that followed, 12 men of the party were bitten and six out of them went down with the disease within 13 days. During the next 5 weeks or so the site remained unoccupied and no cases were reported from this spot. When, after two months, the 'C' Coy. of the same unit occupied it, 3 cases again arrived from the same spot.

In another locality, while advancing, 41 men of a unit took shelter from rain at night in the solitary hut that stood nearby. Within half an hour of sleeping in the hut, they were all so severely bitten that they had to leave it in spite of the drenching rain outside. Of these 15 were admitted to the hospital with fever within the incubation period and one had mild fever but was not hospitalized. None of the associates of these cases, who did not enter the hut, showed any symptoms.

At another spot, where a bunker was built out of the timber from a local dilapidated hut, all the 3 men of one party and 2 of the 4 men from another party who occupied the bunker suffered from the disease within the incubation period. Nearly all the other cases gave similar histories.

All this is in agreement with the recognized features of the disease, i.e. it is a 'house' or 'spot' infection. The infected ticks do not migrate very far and in some instances the histories suggested that one room alone in a house or barrack may be infested. As the parasites pass from one generation of ticks to another, the spot may remain infective for long unless dealt with effectively.

It might be mentioned here that there was enough evidence in nearly all my cases that the enemy, including amongst them Pathans, were

either in occupation of the infective site or that it was constructed out of the timber obtained from the local huts presumably occupied by the enemy.

The ticks do not seem to be liable to transportation in beddings, etc., for, in spite of a systematic search of the equipment of the cases at the rear, no ticks (or lice) were ever found in it.

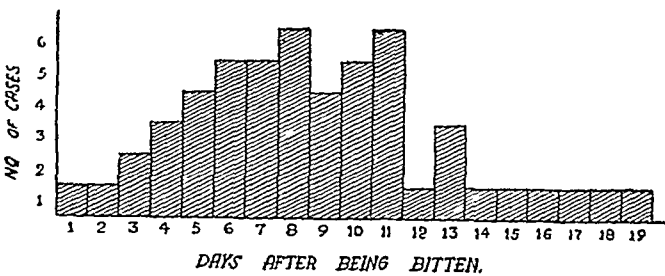
3. Climate

As already stated, the cases recorded occurred from February to mid-June 1948 (after which I left the area, but I understand that a few cases were evacuated even after this). Cases occurred during the months of winter in the valley of Kashmir and in Rajori where temperatures during the rainy days were as low as 30 to 40°F. The province of Jammu recorded a temperature of 108°F. in May 1948 and even during these hot months cases did occur. The seasonal incidents will probably depend on the prevalence of the vector in a particular season. On the evidence before me I do not however wish to comment on this aspect of the disease any further.

4. Incubation period

Figure 1 (graph) gives an idea about the incubation period as recorded in this series. It

Fig. 1.
Incubation period.



will be noticed that 50 per cent cases had an incubation period of 7 to 12 days and 75 per cent cases of 5 to 13 days.

Two cases started with initial fever within 48 hours of being bitten. This fever, however, did not seem, from its symptomatology, to be the true initial fever; but a febrile reaction to the bites and has been classified, amongst others, by Manson-Bahr as tick-bite fever.

5. Prodromata

Immediately after being bitten, the bites started itching. This lasted in my cases for a varying period from 3 to 20 days with an average of 11 days. In 10 (20 per cent) the itching was almost absent during the febrile attack and in 41 (80 per cent) it was continuous.

Within a few hours a small papule with a tiny vesicle at the top appeared. The vesicle was usually scratched off and left a pin-point ulcer which healed rapidly. In a day or two the papules attained the size of a lentil to a split pea, became dark and pigmented, and had a shiny surface and a scaly margin. The earlier lesions were aptly described by one of the patients who said that it appeared as if 'the insect itself had crept under the skin'. In a week or fortnight the lesions became lightnified and deeply pigmented (see figure 5, plate XXVII) and in almost all cases the marks were visible until the discharge of the patients from hospital.

In 10 (20 per cent) cases the fever came on without any other previous symptoms and in 42 (80 per cent) prodromata, lasting from one to five days before the onset of fever, were present.

The chief amongst the prodromal symptoms were malaise (16 cases), giddiness, particularly postural in character (13 cases), anorexia (17 cases) and weakness (16 cases). In nearly all cases these symptoms were mild and the individual carried on at his work in spite of them.

6. Symptomatology

The number of cases showing the various signs and symptoms are shown in table I.

TABLE I
Signs and symptoms

Num- ber Per cent	Itching	Pain			Giddiness			Headache	Malaise	Anorexia	Vomiting			Spleen			Liver			Lymph- adenitis	
		M	S	T	M	S	T				At onset	48 hours	T	P	P Td.	T	P	P Td.	T	R	G.
	51	22	25	47	35	9	44	48	42	42	9	11	20	18	21	39	7	33	40	10	..
	98	42	48	90	67	17	84	88	82	82	17	21	38	25	41	66	13	63	76	16	..

T = Total; M = Mild; S = Severe; P = Palpable; Td. = Tender; R = Regional; G = General.

Itching.—In all undisputed cases, except one, itching was the first and one of the prominent symptoms. In one case however the patient did not complain of any itching in spite of the characteristic bite marks and a positive blood smear. It has been stated by Manson-Bahr that cases who have severe local reactions with itching have either no fever or suffer from a milder attack. This has not been the case in the present series. Ten of the cases who had very intense itching had the severest manifestations of the lot. The other characteristics of the itching have already been described.

Fever is the chief manifestation of the disease. Unfortunately only 15 of the cases came under my observation during the initial febrile stage; but an attempt was made to make a detailed enquiry and collect information from the records, from forward Field Medical Units, accompanying the cases. With the limitations that are natural to such data the following information was gathered.

In 17 (33 per cent) the onset of fever was slow, in 22 (42 per cent) it was sudden with slight chill and in 13 (25 per cent) it was sudden and accompanied by rigor.

Table II shows the duration of the fever and table III the duration of the afebrile intervals between the initial and the subsequent attacks.

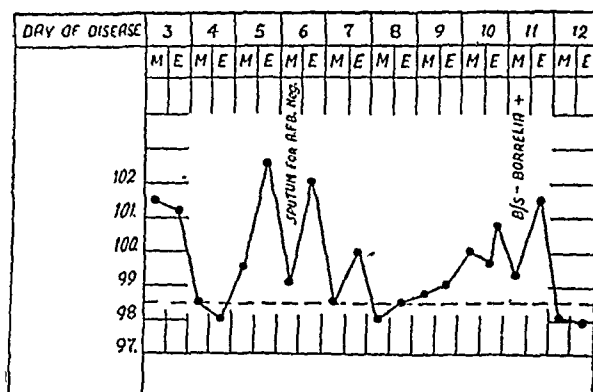
In the large majority the temperature was irregular, being at times remittent and at times intermittent.

This is in marked contrast with the usual textbook descriptions of the disease.

The pulse rate always corresponded to the temperature.

A few typical temperature charts are shown below (see figures 2, 3 and 4).

Fig. 2.



Pain in the body was a prominent feature. In the great majority it was muscular but in

TABLE II
Duration of febrile attacks

	Number of cases observed	Fever lasted for								
		1 day	2 days	3 days	4 days	5 days	6 days	7 days	8 days	9 days
Initial fever	33	8	6	12	2	3	..	2
1st relapse	40	12	11	10	4	2	..	1
2nd relapse	35	10	13	3	9
3rd relapse	11	4	5	2
4th relapse	8	6	1	1
5th relapse	2	1	..	1
6th relapse	1	..	1

TABLE III
Duration of remissions

	Number of cases	Interval in days between various bouts of fever												
		1	2	3	4	5	6	7	8	9	10	12	14	17
Initial fever and 1st relapse.	29	1	3	2	6	7	3	3	..	1	1	1	..	1
1st relapse and 2nd relapse.	21	3	6	3	5	..	1	1	2	1	..	1	1	..
2nd relapse and 3rd relapse.	12	1	3	3	3	1	1
3rd relapse and 4th relapse.	7	1	..	2	3	1
4th relapse and 5th relapse.	2	..	8
5th relapse and 6th relapse.	1	1

a few it was peri-articular. The most characteristic was severe pain in the small of the back and in the neck muscles. Whether this was a manifestation of meningeal or cerebrospinal involvement, as has been suggested by some investigators, cannot be stated. There were, however, no other clinical manifestations of meningeal or cerebrospinal involvement. The pains were only present during fever and cleared up promptly after it subsided.

Fig. 3.

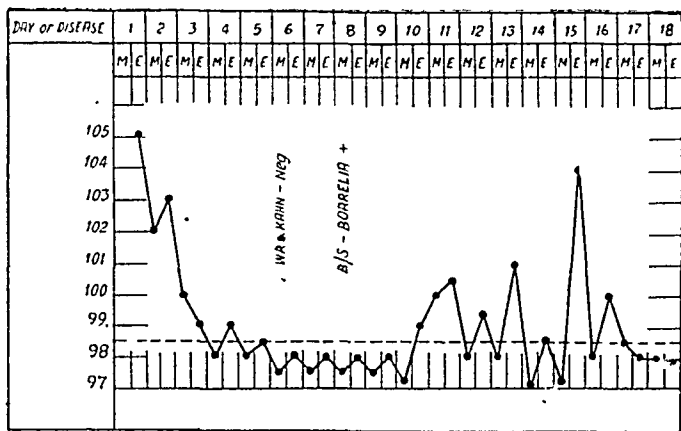
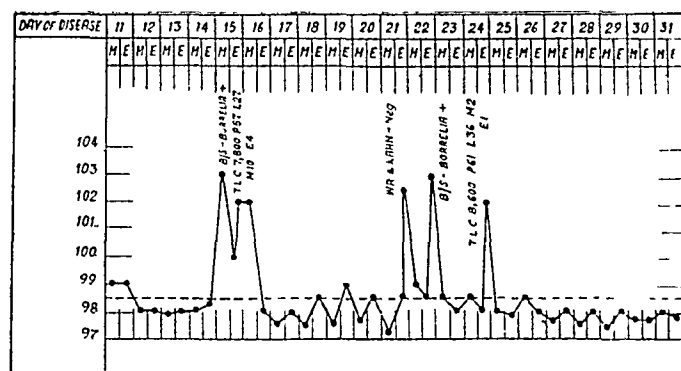


Fig. 4.



Giddiness has been almost a constant symptom in this series. In some it was mild and postural but in the majority it was severe and constant. In one case it was accompanied by a subjective sense of deafness. There were however no objective findings either of labyrinthine or auditory involvement at any stage in any of the cases.

Headache was not a conspicuous symptom. It accompanied fever and varied with its severity, subsiding almost completely after the fever came down. This was in marked contrast with giddiness which was very persistent.

Anorexia and *prostration* were present in the majority of cases. They appeared with the onset of fever and continued throughout the course of the disease. In a few cases these symptoms started in the incubation period.

Vomiting was an insignificant feature and occurred during onset of fever in 8 cases and

after 24 to 48 hours of onset in 11 of the total series. It was always preceded by nausea. In only one case was it intense. This was in marked contrast with cases of malaria and was of assistance in the differential diagnosis.

Sweating during fever, as distinct from critical sweating, occurred in ten cases and was associated with a fall in the fluctuating temperature in them.

7. Signs

Prostration was a noticeable feature in all cases arriving later in the first attack or subsequently. As the disease progressed it became more and more marked and in two cases it was extreme. Cases that came in at the beginning of the first attack of fever did not show any special prostration except for one in whom it was associated with intense vomiting, severe abdominal pain and tenderness above the umbilicus. In this patient it seemed that there was rather a severe involvement of one of the internal organs (probably pancreas), a condition analogous to pernicious malaria. These symptoms responded dramatically to two pints of intravenous glucose saline to which was added 0.45 g. of N.A.B.

Tongue was clear in all cases.

Bite marks were quite characteristic and were present in all cases included in this series. They were present on the exposed parts of the body or their distribution depended on the extent to which the body was exposed at the time of being bitten. The features and evolution of these marks have already been described (see figure 5, plate XXVII).

Icterus was noticeable clinically in only two cases but the icteric index in them varied from 2 to 8 and no bile was detected in the urine.

A peculiar earthy pallor, hard to describe but characteristic in appearance, developed as the disease progressed unchecked. Its intensity corresponded closely to the degree of prostration.

Spleen, the importance of which in a population exposed continuously to malaria may be obviously limited, was in the majority of cases palpable. There was, however, no history of malaria and definite reduction in size occurred before discharge. The presumption of some enlargement consequent on the disease does seem to be justified.

Liver was palpable in 40 cases and in 33 it was also tender.

Lymph nodes, either regional or general, were not appreciably enlarged except in 9 cases where the regional lymph nodes draining the bitten area were enlarged slightly but appreciably.

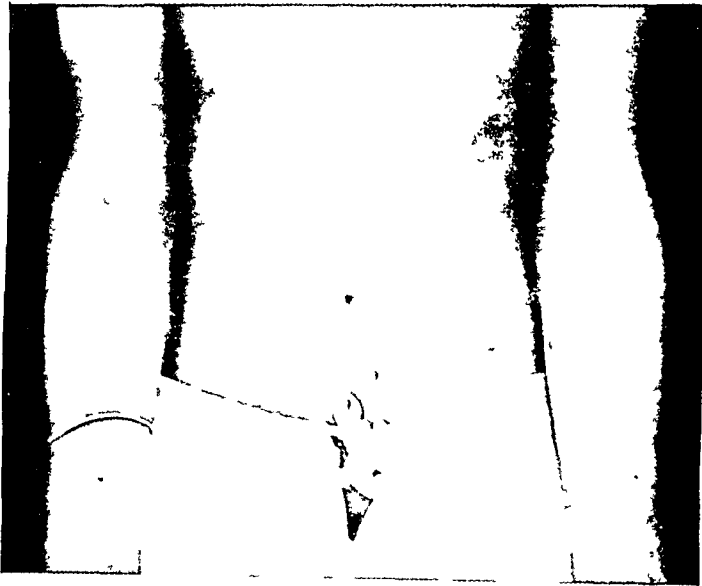
8. Investigation

Blood films unfortunately could not be examined elaborately. An effort was however

PLATE XXVII

RELAPSING FEVER—TICK-BORNE : S. KAUL (O. A.)

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made to examine at least one thick blood smear in all cases daily until the diagnosis was confirmed and during the first few days of treatment. On first admission, three blood slides were examined daily for two days. This entailed a great deal of work but the results obtained justified the time spent. Smears were stained as for malaria. This work was conducted by P. D. Sharma, I.A.M.C., the pathologist in charge of the laboratory.

Of the 108 cases clinically diagnosed, only 52 were smear positive. The stage of disease at which the smears were positive is shown in table IV.

TABLE IV
Results of blood smear examination

CASES OBSERVED						
	Number	Positive		Negative		Final outcome of negative cases
		Number	Per cent	Number	Per cent	
Initial fever ..	13	8	62	5	38	{ + in 1st remission .. 2 cases + " 2nd " .. 2 " + " 4th relapse .. 1 case
1st remission ..	20	7	35	13	65	{ + in 1st relapse .. 10 cases + " 2nd remission .. 1 case + " 2nd relapse .. 2 cases
1st relapse ..	12	6	50	6	50	{ + in 2nd remission .. 3 cases + " 2nd relapse .. 1 case + " 3rd remission .. 1 " + " 4th relapse .. 1 "
2nd remission ..	5	1	20	4	80	{ + in 2nd relapse .. 2 cases + " 3rd " .. 1 case + " 4th remission .. 1 "
2nd relapse ..	3	2	67	1	33	+ in 3rd relapse .. 1 case

From a study of the table it will be evident that of the 28 cases that came under observation for the first time during fever (either initial or one of the relapses), 16 showed positive smears during the febrile stage and 12 remained negative during the first observed bout of fever. Of the 25 cases who came under observation during the first or second remissions, 17 remained negative but 8 were smear positive during the first observed remission. Of all cases observed as many as 18 (30 per cent) were positive for the first time during a remission.

This feature has been an experience in variance with the usually accepted view that the parasites disappear from the blood after the subsidence of fever.

In 4 cases where, for one reason or other, the treatment was not started at once, the smear on an average remained positive for two days. Where repeated smears were taken during a day the parasites persisted in the blood throughout the day.

In the thick films the parasite count varied from 3 to 4 per field to 1 per 10 to 12 fields.

The organism has variously been classified as a spirochæte, spirillum, and borrelia. The varieties carried by the ticks are *Borrelia duttoni* in Central Africa, *Borrelia venezuelensis* in South America, *Borrelia persica* in Persia, *Borrelia marocana* in Marace and a strain in Russia, Turkistan and Palestine. The strains are immunologically different from the louse-borne type.

The strain involved in this series is under investigation by the Army Research Team work-

ing on the subject. No distinctive features about the organism were noticed morphologically.

Total and differential white cell counts could only be undertaken in 16 cases during an attack; of these 3 were repeated before discharge. A study of the findings does not reveal any characteristic deviation in the total or differential counts.

Wassermann reaction and Kahn test were done in 39 cases. Of these 37 were negative and only one showed both Wassermann reaction and Kahn test positive and one showed a Wassermann reaction doubtful and Kahn test negative, syphilis not being a possibility for the positive or doubtful results.

Icteric index, as already stated, was undertaken in two cases suspected of jaundice. In these the icteric index was 4 and 8 respectively.

9. Complications

One case developed acute iritis for which no other cause was found. Two cases had severe

pain in one big joint (one in left knee and one in right elbow) associated with slight effusion. One case appeared to have a severe visceral involvement probably of the pancreas and has already been described. No other complications were noticed in this series. Lumbar puncture was not done in any of the cases.

During the course of illness, one patient developed a relapse of benign tertian malaria concurrently with the disease.

10. Treatment

Two specific therapeutic agents were employed: penicillin and organic trivalent arsenicals. Two schemes of dosage for penicillin were employed. One series of 8 cases was given an initial dose of 50,000 units followed by 30,000 units every three hours for 16 injections by intramuscular route. Another series of 7 cases was given an initial dose of 200,000 units, followed by 100,000 units every three hours for 16 injections by intramuscular route. A third series of 8 cases was given 1.5 g. of N.A.B. (or equivalent dosage of Neo-Helarsin) by intravenous route, starting with a test dose of 0.15 g. as soon as the parasites were found in the blood, irrespective of the stage of illness, followed by two more of 0.45 g. each, at 4 days' intervals.

Blood films in all cases were examined daily until it was thought that a relapse was unlikely. Cases were put on one or the other scheme by turns as they were diagnosed irrespective of the severity of the case. This could however be done only during a certain period, before and after which, on account of administrative and other difficulties, the cases had to be put on the surest line of treatment, i.e. N.A.B. This was unfortunate, as an opportunity for trying further the effect of penicillin was lost.

All cases that showed the parasite or relapsed clinically were given a further course of N.A.B. Relapse rates for the different schemes are given in table V.

From a study of the table it is apparent that penicillin had practically no effect on the disease, 13 of the 15 cases so treated having relapsed.

N.A.B. was tried, in addition to the 8 cases included in the above series, on 29 others and 13 who showed a relapse after penicillin. Of all cases, totalling 50, treated on N.A.B. only, one case had a relapse, needing another injection of 0.45 g. after the completion of a standard course mentioned above. All cases that relapsed after penicillin responded to a course of N.A.B. (The possibility of a natural termination of the disease in some of these cases cannot be ruled out.)

Penicillin has been spoken of very highly in this disease by Greaves *et al.* (1945), Taft and Pike (1945), and Tucker (1946); but its usefulness in this series, although the numbers treated are very small, has been disappointing.

Prolonged courses of penicillin were not tried as it was considered that the misery caused to the patient by the repeated injections was not worth while in the face of a more effective and less troublesome alternative of intravenous organic arsenicals, which in the doses needed for the condition are practically non-toxic. In some cases associated with severe liver or kidney damage, the advisability of using a less toxic substitute like penicillin may arise but as the fundamental cause of such damage is the parasite itself, a sure and swiftly acting remedy which could rid the body of the causal factor should not be replaced by a doubtful agent.

Follow-up cards were given to all patients and later separate letters of enquiry sent to their units. Information was received in only about 37 cases. Seven of these had not joined the unit having been transferred to the dépôts on discharge from base hospitals. Of the remaining 30 cases, one was of the group treated with higher dosage of penicillin and had not relapsed two months after discharge. The other 29 were those treated with N.A.B. and only one of these had relapsed after 20 days of discharge and was re-admitted and given

TABLE V
Effect of treatment

Treatment adopted	Total number treated	Fever with or without positive smear	Positive smear	Clinical relapse	Total relapse	No relapse
Penicillin, small dosage ..	8	2	..	5	7	1
Penicillin, heavy dosage ..	7	1	..	5	6	1
N.A.B. in series with above ..	8	8
N.A.B. otherwise ..	42	.	..	1	1	41

another course of N.A.B. All others had remained afebrile until reported upon, i.e. from 45 days to 60 days after discharge.

11. Discussion and conclusions

The first point of interest that arises is as to what was the source of origin of the outbreak. As stated, a detailed enquiry from medical practitioners, both civil and military, who had worked in the affected areas of Jammu province before the onset of the present disturbances, revealed that no such cases had come to their notice in the past. It is true that with the facilities available to medical men in such out of the way places the recognition of cases may have been difficult; but on the other hand the characteristic tick-bite marks with, in some cases, intense itching, would inevitably draw the attention of the physician to the disease. It is therefore reasonable to assume that the strain was not indigenous.

Further it was noticed that cases started occurring in our troops occupying areas cleared of the raiders. This was conclusively brought out by intimate study of the map at various stages of the operations.

As the troops advanced more and more infected foci came to notice. The same, I presume, happened in Kashmir. None of the undisputed tick-borne cases came from the city of Jammu or other such areas which were at no time occupied by the raiders. This, in spite of large influx of refugees from the affected areas (of course evacuated before they could pick up the infection from the raiders) and the close proximity to our troops, is worthy of note.

No cases of this type were admitted to the civil hospital in Jammu during the period covered by the report, although the civilian medical men were, by then, aware of the incidence in the troops.

All this can admit of only one explanation that the strain was brought in by the raiders. Tick type of relapsing fever is not known either in West Punjab or in India but cases have been said to occur in the tribal territory of N. W. F. and it is highly probable that the strain came from that area.

Another point of interest was the association of 6 relapsing fever cases, not included in the series, who gave a history of having been bitten by bugs or flees. These cases did not show the typical tick-bite marks and appeared not to have been infested with lice at any time. Although they did not come from any known 'spots' of infection, they came, broadly speaking, from the same localities. The point arises whether, besides the ticks, this strain of the borrelia (or any other strain) can be carried by bugs or flees. Transmission experiments alone can elucidate the point.

I should like to mention here that these six cases of relapsing fever who had no history or

marks of tick-bites had symptoms and signs and ran a course indistinguishable from the tick-borne cases.

Summary

An outbreak of relapsing fever (tick-borne) that occurred amongst our troops in the Jammu (and Kashmir) area has been described.

Of the 108 cases clinically typical of the condition only 52 were smear positive, even with a very painstaking search for the parasites.

The symptoms and signs have been analysed. The symptom-complex of 'relapsing' fever with tick-bite marks, severe pains in the muscles, particularly of the back and neck, and persistent giddiness were very characteristic and of diagnostic significance, the last two being of help in differentiation from malaria.

From analysis of cases it has been shown that 32 per cent of cases showed the causal organism in the blood smears for the first time during a remission, a point in variance with the accepted views.

Although the number of cases treated with penicillin has been small, yet in the usual dosage it seems to have had no effect on the strain involved, 13 out of 15 cases so treated having relapsed. Organic trivalent arsenicals, on the other hand, in a dosage of 1.5 g., have been very effective.

This, to my knowledge, is the first outbreak of tick-borne relapsing fever recorded in India and an attempt has been made to prove that the parasitic strain involved was imported by the raiders into the affected area from the tribal territory of N. W. F.

I wish to thank the D.M.S. (India) for permission to publish this note and Lieut.-Colonel B. N. Bhandari, I.A.M.C., for his useful suggestions.

In the end I wish to express my gratitude to Sister Miss E. M. Theophilus, I.M.N.S., for her unremitting help which has made the compilation of this note possible. Thanks are also due to Capt. P. D. Sharma, I.A.M.C., Capt. Narayanan, I.A.M.C., Capt. Narasimhan, I.A.M.C., Mr. S. S. Rajan and the subordinate staff of the Medical Unit at which the work was conducted, for their co-operation and help.

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[Two batches of squashed ticks from Kashmir (not sent by Colonel Kaul), examined by the Serologist to the Government of India, failed to give reaction for human blood. It was later ascertained that they had been collected from animal houses only. They gave reaction for blood of ruminant animals.—EDITOR, *I.M.G.*]

PENICILLIN AS AN AGENT FOR PURIFYING SMALLPOX VACCINE (CALF PROPAGATED VACCINIA VIRUS)

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WITHIN recent years, a great deal of attention has been given to the production of smallpox vaccine free of micro-organisms. Attempts so far made in this direction have not, however, led to the desired result owing to the varying nature of the cultivation of the virus of vaccinia on the open skin surface of the calf. Indeed, this shortcoming of calf propagated vaccinia virus has led to the development of methods for the production of bacteria-free vaccinia virus in tissue culture and in the developing chick-embryo. Attempts to free the calf propagated vaccinia virus of all associated micro-organisms have been made in the past mainly by means of suitable chemicals, although physical agents such as x-rays have also been employed by Levin (1935). The main difficulty in the matter of purification of calf lymph vaccine has been that immunity to smallpox or its allied disease can be conferred, it appears, only by living virus. Attempts to induce immunity with inactivated virus (heated or treated with chemicals) have not been attended with much success (Parker and Rivers, 1936), though this is ascribed by Smith *et al.* (1948), to some extent, to the difficulties of obtaining preparation of sufficient virus concentration. These authors claim that completely inactivated virus in sufficient concentration may be effective in some instances. Various methods of purification of vaccinia virus that are in vogue are not reliable in freeing the lymph, particularly freshly prepared lymph, entirely of contaminants without reducing its potency.

In this Institute, however, penicillin is used with satisfactory results, as an agent for purifying glycerinated calf lymph vaccine. Records of recognized tests for purity and potency of penicillin-treated vaccine lymph, together with records of results achieved, show conclusively that penicillin is a potent and reliable agent in

freeing the lymph entirely of the commonly occurring extraneous organisms, provided the lymph does not contain organisms such as *B. coli* which are not susceptible to penicillin and spores of spore-bearing aerobes and anaerobes. If *B. coli* is found as a contaminant of calf lymph vaccine, the only way to get rid of it is to store the lymph for a considerable time at a temperature below -10°C . Bacteriological tests of hundreds of lymph numbers in this Institute have not however revealed the presence of this organism as a contaminant in any of the samples, although this does not mean that routine test need not be done on this account for the detection of the organism in vaccine lymph. Similarly the spores of Gram-positive spore bearers are not affected by penicillin (although their vegetative forms are susceptible to it).

As queries are being received by the author regarding the exact method of purifying calf lymph vaccine by means of penicillin, the technique followed in this Institute is described below for the information of those interested in the subject.

Technique

Before going into the details of the actual process of treating vaccine lymph with penicillin, it is considered essential to stress at the outset that whatever method of purification is followed, the importance of rigid sanitation at every stage of preparation of vaccine cannot be over emphasized.

The vaccine pulp collected in sterile, tared glass phials from calves 120 hours after inoculation is weighed and stored in the freezer to await processing. Twenty-four hours after collection from calves, the frozen pulp is passed successively through two sets of sterile mechanical lymph grinding machines for coarse and fine grinding, and is ground to a smooth consistency with the addition of sterile 50 per cent re-distilled glycerine in distilled water. The grinding machines used in this Institute are Baird and Tatlock's coarse grinding laboratory mill, Felix-Fluck triturating machine (Lausanne) and Doring lymph grinding machine; recently a Waring Blender has also been introduced. The glycerine used is chemically pure, free from mineral acids and has a sp. gr. of 1.260 as originally advocated by Copeman (1899) and a pH of 7. pH 8 is more destructive to vaccinia virus than pH 6 or 7. Therefore, 50 per cent glycerine and water mixture before sterilization is titrated with sodium bicarbonate to adjust the pH to 7.4 to remove any acid reaction which is destructive to the virus. After sterilization by autoclaving, the pH becomes 7.2.

The finely ground lymph is further mixed with 50 per cent glycerine and water mixture to make a dilution of 1 to 2 and this mixture is tested for purity and potency. The detection, with confirmation, by animal inoculation of *B. anthracis* and *Cl. tetani* is the cause for

rejection of the lymph at this stage. If found free from these organisms phenol is added to lymph in 0.75 per cent strength and the lymph is stored in the freezer at -12°C . Depending upon the urgency of demands, usually after six weeks to about six months of such storage in the cold, this lymph is finally diluted 1 to 4 by the addition of further quantities of 50 per cent glycerine and water mixture containing the requisite dose of penicillin. The final concentration of phenol in the purified lymph is 0.44 per cent; phenol is found useful in preventing the growth of moulds which are not affected by penicillin. It has been our experience that a dose of 100 units or over of penicillin per 1 cc. of lymph diluted 1 to 4 is usually certain to clear such a lymph of all contaminants, in other words 450 units of penicillin are required per gramme of lymph (0.99 cc. of glycerine = 1 gramme of pulp by weight).

This penicillin-treated lymph contained in sterile neutral glass bottles is next vigorously shaken for a minute to effect thorough and uniform mixing of the penicillin solution with the lymph. The shaking is best carried out by an electrical shaking machine. Twenty-four to forty-eight hours after treatment with penicillin the lymph is again put through the tests for purity and potency conforming to the Drug Rules and is finally clinically tested on unvaccinated children. This lymph should be used up within two months from the date of completion of purity and potency tests. If not used up, it should be retested for purity and potency before it is passed for issue.

The results of tests for purity of penicillinized lymph and of the potency of lymph before and after treatment with penicillin are set out in tables I and II respectively.

In this Institute, potency is tested on calf or rabbit whatever is available, according to the following methods.

(A) *On calf*.—Cunningham's test with a vesiculation factor above 2 in a dilution of 1 in 1,500.

The lymph is diluted 1 in 1,500 in physiological salt solution; the dilution is sown on a calf in series of five horizontal lines one above another and each one inch long, one dip of the knife in the lymph being used for each line. The result is read at 120 hours as under :—

(a) Continuous vesiculation along all the lines = 'Continuous'.

(b) Continuous vesiculation along a minimum of three lines and discrete vesicles on the remaining line = 'Almost continuous'.

(c) Discrete vesicles in all lines. Vesicles are counted and the number divided by the total length of the five incisions. This gives the vesiculation factor, i.e. the number of vesicles per inch. Example: if the number of vesicles counted is 10, then $10/5 = 2$ which is the V.F.

A lymph showing a vesiculation factor of less than 2 is discarded.

(B) *On rabbit*.—Stevenson's modification of Calmette-Guérin method (Stevenson and Butler, 1936); lymph is diluted 1 in 1,000 in physiological salt solution and 0.1 cc. of the diluted lymph is inoculated on the shaved back of a healthy, young, unvaccinated rabbit about six months old, on an area 7 cm. \times 2 cm. Two rabbits are usually used for each test, since individual animals vary greatly in their relative susceptibility to the vaccine. But if there is time to wait, one rabbit is inoculated first and in case there is no reaction, a second rabbit is inoculated later.

An eruption of confluent vesiculation over the field of inoculation is usually produced in 5 days. Discrete vesicles are obtained in higher dilutions such as 1/5,000 or 1/10,000. Some very potent lymphs have given confluent reaction even in 1 in 10,000.

Penicillin used is crystalline penicillin G sodium manufactured by the following firms :

- (1) Parke, Davis & Co., U.S.A.
- (2) Glaxo Laboratory Ltd., England.
- (3) E. R. Squibb & Sons, U.S.A.
- (4) Commercial Solvent Corporation, U.S.A.
- (5) Chas. Pfizer & Co., U.S.A.

Results and discussion

Results obtained with penicillin-treated glycerinated calf lymph vaccine have been quite satisfactory as will be evident from the results obtained from the vaccinators (*vide* table II). In this connection it is also emphasized that vaccination work in this province is not confined to the cold weather but is carried out throughout the hot season as well. Very high temperatures are recorded during the hot months of the year—April, May and June—when the maximum temperature varies from 108°F . to 116°F . Further it has been observed that vaccination with this penicillin purified glycerinated calf lymph, free from all extraneous organisms, is attended with marked absence of inflammation in the surrounding tissues and firm vesicles are obtained about the seventh day of vaccination. Table I shows that doses of penicillin varying from 50 to 102 units per cc. of lymph diluted 1 in 5 have been used. In some of the samples (serial nos. 14 to 18) where the initial counts of the untreated lymphs were already low (between 2,000 to 4,000 colonies per cc.), due to prolonged storage at 12°C ., doses as low as 22 units per cc. were found sufficient to clear the lymphs of all growths, while in the case of the serial nos. 26 to 29, where the lymph numbers were treated with penicillin immediately after manufacture, 50 units of penicillin per cc. of lymph in each case were found adequate although the corresponding unpenicillinized samples showed innumerable colonies. It might be of interest to

TABLE I

Serial number	Lymph number	Quantity in cc.	Date of manufacture	Date of treating with penicillin	Dose of penicillin in units per cc.	Date of inoculation	BACTERIOLOGICAL TESTS				
							Results				
							After 24 hours	After 48 hours	After 5 days.		
							N.B.	P.C.	G.B.	C.M.	L.M.
1	M 29	699	10-11-47	30-1-48	64	31-1-48	0	0	0	0	No change
2	M 30	598	10-11-47	30-1-48	64	31-1-48	0	0	0	0	Do.
3	M 31	581	10-11-47	30-1-48	64	31-1-48	0	0	0	0	Do.
4	M 33	606	10-11-47	30-1-48	64	31-1-48	0	0	0	0	Do.
5	M 34	502	10-11-47	13-2-48	80	31-1-48	0	0	0	0	Do.
6	M 35	702	25-11-47	20-2-48	80	31-1-48	0	0	0	0	Do.
7	M 39	662	8-12-47	20-2-48	80	21-2-48	0	0	0	0	Do.
8	M 53	965	22-12-47	12-3-48	77	16-3-48	0	0	0	0	Do.
9	M 54	719	22-12-47	12-3-48	77	16-3-48	0	0	0	0	Do.
10	M 55	773	22-12-47	12-3-48	77	16-3-48	0	0	0	0	Do.
11	M 56	892	23-12-47	12-3-48	77	16-3-48	0	0	0	0	Do.
12	M 57	565	23-12-47	12-3-48	77	16-3-48	0	0	0	0	Do.
13	M 59	716	29-12-47	31-3-48	76	2-4-48	0	0	0	0	Do.
14	M 78	982	27-1-48	4-9-48	22	8-9-48	0	0	0	0	Do.
15	M 79	995	2-2-48	4-9-48	22	8-9-48	0	0	0	0	Do.
16	M 80	916	2-2-48	4-9-48	22	8-9-48	0	0	0	0	Do.
17	M 81	655	2-2-48	4-9-48	22	8-9-48	0	0	0	0	Do.
18	M 82	1,000	3-2-48	4-9-48	22	8-9-48	0	0	0	0	Do.
19	M 83	831	3-2-48	11-9-48	64	14-9-48	0	0	0	0	Do.
20	M 94	930	9-2-48	11-9-48	64	14-9-48	0	0	0	0	Do.
21	M 1	936	23-8-48	9-11-48	102	19-11-48	0	0	0	0	Do.
22	M 2	901	23-8-48	17-11-48	102	19-11-48	0	0	0	0	Do.
23	M 3	988	23-8-48	17-11-48	102	19-11-48	0	0	0	0	Do.
24	M 4	819	23-8-48	17-11-48	102	19-11-48	0	0	0	0	Do.
25	M 17	880	20-9-48	14-12-48	89	21-12-48	0	0	0	0	Do.
26	M 78	204	3-2-49	3-2-49	50	6-2-49	0	0	0	0	Do.
27	M 79	492	7-2-49	7-2-49	50	10-2-49	0	0	0	0	Do.
28	M 85	424	21-2-49	21-2-49	50	24-2-49	0	0	0	0	Do.
29	M 86	486	21-2-49	21-2-49	50	24-2-49	0	0	0	0	Do.

N.B. = Nutrient broth.

P.C. = Agar plate count.

G.B. = Glucose broth.

C.M. = Robertson's cooked meat medium.

L.M. = Litmus milk.

0 = Sterile (no growth).

remember in this connection that penicillin is particularly active against young bacterial cells (Kolmer, 1947). The practice at the present moment, in this Institute, based on our experience, as has already been stated, is to use not less than 100 units of penicillin per cc. of lymph diluted 1 in 5.

Potency is the next question. Penicillin in the doses used did not affect the potency of the lymph in any case (*vide* table II). Further noticeable fact is that the potency of the penicillinized lymph did not deteriorate even eleven months after treatment with penicillin when such lymph samples were stored at -12°C .

Summary and conclusions

A method has been described for the rapid purification of glycerinated calf lymph vaccine

by means of penicillin. Penicillin has been found to be a powerful agent in rapidly freeing the lymph—even freshly prepared lymph (table I, serial nos. 26 to 29) of the commonly found extraneous organisms without affecting the potency of the virus in the dosage used; thus a pure product can be in the hands of vaccinators within two weeks from the date of collection of lymph. The results of vaccination on children with penicillin-purified glycerinated calf lymph vaccine were found satisfactory (table II).

The author wishes to express his thanks to the Director of Public Health, Central Provinces and Berar, Lieut.-Colonel A. S. Garewal, for his keen interest and encouragement in the preparation of this paper. Opportunity is also taken to thank the staff of the C. P. Vaccine and Public Health Institute, particularly Messrs. B. G. Naidu and M. S. Dahikar, for their assistance in completing the records.

TABLE II

Serial number	Lymph number	POTENCY TESTS						Date of despatch to vaccinators	Total number of children vaccinated	RESULTS RECEIVED FROM VACCINATORS	
		Unpenicillinized lymph			Penicillin-treated lymph					Case success rate per cent	Insertion success rate per cent
		On calf			On calf						
		Date of test	Dilution	Result at 96 hours	Date of test	Dilution	Result at 96 hours				
1	M 29	30-1-48	1 in 1,500	Almost continuous.	9-2-48	1 in 1,500	Continuous	17-2-48	572	98	88
2	M 30	30-1-48	Do.	Do.	9-2-48	Do.	Do.	18-2-48	177	95	89
3	M 31	30-1-48	Do.	Do.	9-2-48	Do.	Do.	20-2-48	1,396	92	83
4	M 33	30-1-48	Do.	Do.	9-2-48	Do.	Do.	25-2-48	430	100	92
5	M 34	30-1-48	Do.	Do.	26-2-48	Do.	Do.	1-3-48	108	96	63
6	M 35	30-1-48	Do.	Do.	26-2-48	Do.	Do.	2-3-48	248	96	82
7	M 39	30-1-48	Do.	Do.	26-2-48	Do.	Do.	28-2-48	123	100	93
8	M 53	4-3-48	Do.	Continuous	17-3-48	Do.	Almost continuous.	1-4-48	2,194	97	87
9	M 54	4-3-48	Do.	Do.	17-3-48	Do.	Do.	6-4-48	1,259	99	92
10	M 55	4-3-48	Do.	Do.	17-3-48	Do.	Do.	12-4-48	1,418	98	93
11	M 56	4-3-48	Do.	Almost continuous.	17-3-48	Do.	Do.	16-4-48	1,412	98	86
12	M 57	4-3-48	Do.	Do.	17-3-48	Do.	Do.	22-4-48	866	97	92
13	M 59	21-3-48	Do.	Do.	17-3-48	Do.	Do.	26-4-48	1,863	98	90
14	M 78	2-9-48	Do.	Continuous	8-9-48	Do.	Continuous	28-9-48	1,135	99	93
15	M 79	2-9-48	Do.	Do.	8-9-48	Do.	Do.	29-9-48	845	98	88
16	M 80	2-9-48	Do.	Do.	8-9-48	Do.	Do.	1-10-48	618	98	91
17	M 81	2-9-48	Do.	Do.	8-9-48	Do.	Do.	4-10-48	1,164	95	90
18	M 82	2-9-48	Do.	Do.	8-9-48	Do.	Do.	6-10-48	2,333	98	90
19	M 83	2-9-48	Do.	Do.	15-9-48	Do.	Do.	11-10-48	933	95	91
20	M 84	9-9-48	Do.	Do.	15-9-48	Do.	Do.	11-10-48	1,337	98	92
21	M 1	25-8-48	Do.	Do.	9-11-48	Do.	Do.	30-11-48	2,885	93	90
22	M 2	25-8-48	Do.	Do.	9-11-48	Do.	Do.	1-12-48	2,308	97	88
23	M 3	25-8-48	Do.	Do.	9-11-48	Do.	Do.	3-12-48	1,420	93	89
24	M 4	25-8-48	Do.	Do.	9-11-48	Do.	Do.	4-12-48	1,635	93	93
25	M 17	29-9-48	1 in 5,000	Do.	16-12-48	1 in 5,000	Do.	21-9-49	911	99	89
On rabbit											
26	M 44	Not done			3-3-48	1/1,000	Confluent	11-3-48	210	97	89
27	M 45	Do.			3-3-48	1/10,000	discreet.	12-3-48	336	100	94
28	M 46	Do.			3-3-48	Do.	Do.	15-3-48	222	99	86
29	M 47	Do.			3-3-48	Do.	Do.	16-3-48	267	98	90
30	M 48	Do.			3-3-48	Do.	Do.	17-3-48	73	100	96
31	M 49	Do.			3-3-48	Do.	Do.	19-3-48	411	93	75
32	M 50	Do.			3-3-48	Do.	Do.	23-3-48	213	97	87
33	M 51	Do.			3-3-48	Do.	Do.	27-3-48	192	98	83

TABLE III

Serial number	Office copy of lymph number	Date of manufacture of lymph	Date of treatment with penicillin	Date of potency test after treated with penicillin	Date of despatch to vaccinators	POTENCY TEST ON OFFICE COPIES OF LYMPH NUMBERS ON CALF		
						Date of test	Dilution	Result
1	M 53	22-12-47	12-3-48	17-3-48	1-4-48	9-2-49	1 in 1,500	Continuous.
2	M 54	22-12-47	12-3-48	17-3-48	6-4-48	9-2-49	Do.	Do.
3	M 55	22-12-47	12-3-48	17-3-48	12-4-48	9-2-49	Do.	Almost continuous
4	M 56	23-12-47	12-3-48	17-3-48	16-4-48	9-2-49	Do.	Do.
5	M 57	23-12-47	12-3-48	17-3-48	22-4-48	16-2-49	Do.	Continuous.

TABLE IV
Result of purity tests on lymph samples penicillinized immediately after manufacture

BACTERIOLOGICAL TESTS																
Serial number	Lymph number	Date of manufacture	Quantity in cc.	Before purification with penicillin				After purification with penicillin								
				Date of test	Results				Penicillin added in units per cc.	Date of adding penicillin	Results					
					After 48 hours	After 5 days					Date of test	After 24 hours	After 48 hours	C.M.	G.B.	L.M.
						P.C.	P.C.	G.B.								
1	M 77	1-2-49	529	4-2-49	++++	G.T.	G.	0	1-2-49	50	4-2-49	0	0	0	No change	
2	M 78	3-2-49	204	6-2-49	++++	Do.	Do.	0	3-2-49	50	6-2-49	0	0	0	Do.	
3	M 79	7-2-49	492	10-2-49	++++	Do.	Do.	0	7-2-49	50	10-2-49	0	0	0	Do.	
4	M 80	7-2-49	474	10-2-49	++++	Do.	Do.	0	7-2-49	50	10-2-49	0	0	0	Do.	
5	M 81	7-2-49	204	10-2-49	++++	Do.	Do.	0	7-2-49	50	10-2-49	0	0	0	Do.	
6	M 85	21-2-49	424	24-2-49	++++	Do.	Do.	0	21-2-49	50	24-2-49	0	0	0	Do.	
7	M 86	21-2-49	486	24-2-49	++++	Do.	Do.	0	21-2-49	50	24-2-49	0	0	0	Do.	
8	M 87	21-2-49	350	24-2-49	++++	Do.	Do.	0	21-2-49	50	24-2-49	0	0	0	Do.	

P.C. = Agar plate count.
C.M. = Robertson's cooked meat medium.
G.B. = Glucose broth.
L.M. = Litmus milk.
N.B. = Nutrient broth.

++++ = Innumerable.
G.T. = Gas and turbidity.
G. = Gas.
0 = Sterile (no growth).

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(See Correspondence, *I.M.G.*, August 1949, p. 379.—
EDITOR, *I.M.G.*)

A Mirror of Hospital Practice

ANAPHYLACTIC SHOCK

By P. K. GHOSH, M.D.

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THAT the development of anaphylactic shock is possible any time during a course of injections of substances liable to produce the reaction is clearly evidenced by the following case recently treated by me.

A Sikh lady, aged over 50, received two courses of milk injections for eczema. Before starting the second course, she was tested for anaphylactic reactions and was found negative to the test. She took 5 injections of lactoprotein (B.L.) twice a week without any trouble. About 15 minutes after the last injection of the course, of 10 cc., she suddenly developed severe anaphylactic shock. She was cold, clammy, almost unconscious with stiff body, fixed pupils insensitive to light or touch, almost imperceptible pulse and cadaveric face. Stimulant inhalations, draughts and 1 cc. 1 in 1,000 adrenalin (Evans') failing to show any improvement, coramine 1.7 cc. was given intravenously. This produced the desired effect and her subsequent recoupment was uneventful. She is in good health now.

A CASE OF RABIES

By M. HATANGDI, M.B., B.S., D.T.M.
Lady Jackson Hospital, Dohad

Mrs. H. I., a Muslim female of 52 years, was bitten by a dog, said to be 'mad', on 2nd April, 1949, in the city of Dohad. She was bitten, unprovoked, on the left forearm and on the abdomen in the pubic and right inguinal regions. The bites on the forearm were on bare skin and those on the trunk were through clothing. There were twelve teeth marks, all drawing blood, some being superficial grazes and others being deep. All the bites were cauterized and later on dressed daily with 1 in 1,000 acriflavin solution. Class III treatment (10 cc. of anti-rabic vaccine by deep subcutaneous injection daily for 14 days) was instituted on the very first day, within about 4 hours of the bite, and duly completed on 15th April, 1949. Nothing untoward happened during the course and the bites too healed satisfactorily. Four days later on 19th April, 1949, she was again brought to the hospital as she was said to be behaving 'strangely' at home. She was said to have been getting into increasingly profound moods of depression during which she would be morose, talk to no one, sit in a corner all by herself for hours together, neither eat nor drink and at times cry softly; these moods alternated with ones in which she was very excitable, talking at random and would shriek all of a sudden as if with some mortal terror, and keep on saying that she was soon going to die and be with Allah. She would ask for food and drink but actually partake of very little saying that there was a devil in her throat who prevented her from swallowing. She complained of severe headache and slight fever. This had been going on for 3 days and she was treated with home remedies.

On examination, it was noted that she had excessive salivation, trembling of the lips and tongue with a slurring and stammering speech, tremors of the hands and a slight but definite exaggeration of the deep jerks on both sides. The pupils dilated and sluggish in reaction. She was restless and appeared to have some difficulty in breathing though there was no cyanosis or cardiac distress. There was no muscular rigidity but she complained of cramps in the thighs and legs. The bitten areas had completely healed and showed no signs of breaking down, nor were they tender or inflamed. She was given a glass of water to drink; the first two mouthfuls were taken slowly and with apparent difficulty. Then she put the glass down and would drink no more. The typical hydrophobic deglutitory spasm was absent. She had no fever but the pulse was fast, being 110 per minute. There were no clinical signs pointing to any other disease and she was diagnosed as a case of hydrophobia, possibly 'modified', as far as clinical features were concerned. She was given a bromide chloral

development. The grubs that are destined to become future queens are fed lavishly and for a longer period on royal jelly. Such larvæ grow double the size of worker bees, develop large ovaries and mature sex glands and in later life are capable of laying eggs. The worker bees on the other hand are fed mostly on pollens and nectar and hence emerge with infantile sex glands incapable of function. Obviously royal jelly plays an important rôle in the development of sex function of bees.

The extract from royal jelly, when injected into the immature rats, produces a definite increase in weight of ovaries by about 60 per cent and the ovaries show a microscopic evidence of strong follicular stimulation as compared with control animals. This interesting observation is worth further investigation as it promises to be of considerable value in gynaeco-pharmacology.

2. The bee sting and bee venom

(a) *The bee sting.*—The stinging system of bees is a very complicated organ. It is a modified ovipositor. It consists of a piercing apparatus, the lateral plates, the appendages, the poison sac and the poison glands. This system is situated between the oviduct and the rectum. The piercing apparatus of the sting is situated ventrally and consists of a sheath and a dart lying within the sheath. The distal one-third of the dart possesses a series of barbs whose shape may aptly be compared to the tip of a crochet needle. The barbs may vary from 6 to 10 in number. When the bee stings these barbs follow the dart and fix the sting in position into the wound. Usually a bee stings the victim with great force and the sting is buried deep into the skin and when the bee flies away the sting with whole of the stinging apparatus is torn off from the body of the bee and is left into the wound. The sting can be lifted out of the wound by a lever action of the finger nails or with the edge of a sharp knife applied at the sides of the wound. The sting should not be pressed as in that case the poison gland bursts and its contents get into the part stung. If the sting is removed without injuring the poison bag, there will not be much irritation or swelling. The bee stings frequently and most viciously at the end of summer when honey is being guarded. During winter the potency of stings sinks rapidly (Coke, 1934).

(b) *Chemistry and bacteriology of the venom.*—Bee venom is a clear watery liquid with sharp bitter taste, aromatic odour and is distinctly acid in reaction. The specific gravity of bee venom is 1.13. It is highly soluble in water and acids and is almost insoluble in alcohol. It contains about 30 per cent of solid matter. Bee venom contains 4.36 per cent carbon, 13.6 per cent nitrogen, 7.1 per cent hydrogen and 0.6 per cent of sulphur. The weight of an average drop of venom is about 0.2 to 0.3 mg. When dried it is converted into a gum-like substance without

loss of potency. It is thermostable and can stand a temperature of 100°C. for 10 days. Prolonged boiling makes the clear venom distinctly cloudy. If it is boiled in a sealed glass tube even for 2 hours its appearance is not affected. Bee venom is colloidal in nature and cannot be dialysed through a membrane. It is destroyed by oxidizing agents as potassium permanganate, potassium sulphate, chlorine and bromine. Alcohol has a strong destroying action on it. Bromine, iodine and ammonia neutralize it. Pieric acid, chromic acid and carboic acid also fix it up locally and destroy its action. Alkalies break bee venom into its components.

The venom, as a rule, is free from bacteria and to a certain degree prevents their growth. The venom and bacteria are mutually destructive but the former is more potent of the two. While venom is normally bacteria-free, it is not considered as a powerful antiseptic. According to Langer 0.1 per cent solution of bee venom retards the growth of streptococci. If a culture of streptococci is exposed to the action of bee venom for a certain period and then removed to an indifferent solution, it regains its original virulence, thereby showing that the venom only retards the activity of the growth of cocci.

Sulphydryl compounds such as reduced glutathione or sodium thiolactate at certain hydrogen ion concentrations oxidize the bee and the cobra venom (Binet, Weller and Robillard, 1939).

(c) *Methods of collection of bee venom.*—The original method of bee venom therapy is to induce the bees to sting a rheumatic patient at or about the painful site. From one to ten stings are used. This method, though simple in its technique, has its own limitations, since the bees are not available at all the places and in all seasons. The physician cannot have the bees always at his command in his medical bag, nor can the dose of the venom thus injected be well regulated. Below are some of the methods used for the collection of bee venom as suggested by Beck (1935).

1st method:—Press carefully the lower part of the bee's abdomen with thumb and index finger. By this procedure the sting protrudes out, and a clear drop of venom becomes visible at the end, which can be collected in capillary tubes or absorbed on to a blotting paper or flushed off in normal saline solution. By careful handling bees can be used repeatedly and venom collected without injuring the stinging apparatus. This method is not practical for collection of venom on a large scale as it is slow and tedious.

2nd method:—Put the bees on a heavy and wet blotter. They sting it immediately and poison discharged is absorbed into the paper. This method is very simple and successful though laborious. With a little experience and practice the venom can be collected from several thousand bees in one day. The venom-soaked paper is dried and kept in a well-closed jar. In this way an albuminous venom is obtained which can be preserved for years. To the watery extract of this venom about one-third or half volume of glycerine is added as a preservative.

3rd method:—Press the abdomen of bees and pull out the protruding sting with fine forceps. Otherwise

the whole lot of bees are killed with chloroform and the protruding stings at the rear end of the abdomen can be easily pulled out with fine forcep. The whole stinging apparatus consisting of gland, poison sac, muscle and chitin are thus pulled out along with the sting. Place these stings in 90 per cent alcohol and let the mass coagulate. Strain the alcohol through a funnel. Dry the stings at 40°C. Rub the dried stings into a fine powder and make an extract in several cc. of distilled water, concentrate and add glycerine as a preservative. One thousand stings thus collected and dried weigh about 2/3 gm. and about 0.03 to 0.15 gm. of venom can be extracted.

4th method :—Divide a swarm of about 25,000 bees into several sections. Put them into large glass vessels. Cover the opening of the vessels with a blotting paper on which pour ether. The ether fumes irritate the bees, who discharge their venom in excitement. Some of the venom remains on the glass vessel and a certain quantity sticks on to their bodies. When the bees are in deep narcosis the vessel and the bees are washed off with distilled water to bring the venom into solution which is later on concentrated. Flury has obtained 50 to 75 mg. of venom from a thousand bees.

(d) The effect of diet on the production of venom.—It has been observed that the quality and quantity of the venom secreted not only depend on the types of bees but also on the variety of their food. As the main active principle of bee venom (neurotoxic action) is a nitrogenous substance, a proteose, it was considered necessary to determine whether the yield of venom could be improved by making the diet of bees higher in proteins. Lauter and Vrla (1939) showed that pollens (a rich protein diet) play an important part in the diet of bees and the production of venom. The intestines of bees from 3rd to 10th day of their development are full of pollens and from 11th to 20th day the pollen contents of the gut is reduced. During the first 5 days of their life, they produce on the average 51 gamma of dried venom and at the age of 25 days (adult life) produce on the average 110 gamma of dry venom. These authors took up the study of different factors which might influence the secretion of venom. Their investigations have shown that in addition to sugar and honey bees require a diet partly composed of proteins in order to secrete a good type of venom. They demonstrated that bees kept on pure sugar diet during the 1st to 10th day of their life produced 18.5 gamma of venom (per bee) while those which had ample access to pollens produced on the average of 79 gamma of dried venom (roughly equivalent to 0.237 mg. of natural liquid venom). The table below gives the effect of diet on the secretion of venom :—

(e) Standardization and sterilization of bee venoms.—It has been mentioned above that the venom as a rule is free from bacteria. But before it is prepared and standardized for parenteral therapy it is necessary to see that it is not contaminated. Chopra, Chowhan and Chopra (1942) suggested various methods for the sterilization of venom preparations. The technique for the sterilization and standardization as suggested by the authors may also be used for the bee venom preparations. The standardization of venoms consists in determining the maximum tolerated and the minimum lethal dose in 24 hours, for white mouse, weighing about 20 grammes, when injected intramuscularly. Lauter and Griggs (1939) collected the bee venom and standardized it by administering it intravenously to white mice. The M.L.D. was found to be approximately 79 mg. per 20 gm. of mouse. They further reported that 22 gamma of this venom haemolysed 0.1 cc. of washed red blood corpuscles, suspension of rabbit and 20 gamma in normal saline showed a definite necrotic action when injected intracutaneously.

(f) Pharmacology and therapeutic uses of bee venom.—The present author has already reported (1938) the pharmacological action of bee venom in some details. Bee venom like cobra venom contains a neurotoxin, a haemolysin and endotheliotoxin. It may be stated briefly that in concentration of 1 to 1,000 bee venom retards the growth of streptococci. Intravenous injection in experimental animals produces a fall of blood pressure, reduction of kidney volume, and increases of limb volume. It produces a marked contraction of isolated virgin uterus of guinea-pig and other smooth muscles and the action resembles that of histamine. It produces leucopenia, decrease of erythrocytes and a marked haemolysis of R.B.C. This action appears more or less to be similar to that of rattlesnake venom.

It has been observed that people engaged in bee farming industry are rarely affected by rheumatism and malignant growths. Bee venom has been shown to cure successfully experimentally produced cancer in rabbits. Bee sting as a curative for rheumatism is a well-known time-old remedy. The mode of action of bee venom in this condition is still obscure, though there is a considerable evidence of its value. The anti-rheumatic action of venom is probably due to

Days of life	NATURAL DIET		ARTIFICIAL DIET	
	Dried venom (gamma)	Equivalent liquid venom (mg.)	Dried venom (gamma)	Equivalent liquid venom (mg.)
5	51	0.153		
10	79	0.237	Decreased	Decreased
25 (adult)	110	0.330	18.5	0.056

the stimulation of the metabolic processes of the tissues leading to a breakdown and elimination of the toxic products. Bee venom is administered intracutaneously in increasing doses at an interval of few days over a period of a few weeks, or in the form of an ointment applied locally at the site. There may be a temporary local irritation and redness, pyrexia, drowsiness and dizziness. Bee venom is useful in rheumatic endocarditis, rheumatic iritis, neuralgias and rheumatic condition of joints and muscles. Various bee venom preparations are available in the market as *Apicur*, *Forapin*, *Apicosan*, *Immenin*, *British Bee Venom* and *Apisin*.*

It has been stated above that the bee sting can be easily lifted out of the wound with the edge of a sharp knife or with finger-nails without the poison bag of the sting being injured. Bee venom is also neutralized by strong alkalis, ammonia, carbolic acid and iodine. Binet and Burstein (1940) suggest that sulphydryl compounds such as reduced glutathione and sodium thiolactate at certain hydrogen-ion concentration may be used as a local application to fix and neutralize the venom in cases of extensive bee stings. Their experiments also justify the use of adrenaline and ephedrine for severe general reactions produced in venom poisoning. A further work in the chemical neutralization of venom is being carried out.

3. Propolis (bee glue)

Bee glue, known as *sitha* (Hindustani), is a dark brownish grey resinous substance found deposited at the base of beehive. It is stated to be collected by the worker bees from the resinous exudate of buds of various trees such as the balsams, poplars and conifers. Bees used this glue to seal the outlet of the cells of the hive. Bee glue is aromatic in odour and brittle when cooled. It melts at 105°F. It sinks in water while beeswax floats. It is soluble in alcohol, turpentine, ether and chloroform. The indigenous physicians use it as a local application in order to ripen the deep abscesses and chronic ulcers. It may be useful in various other pathological conditions.

4. Beeswax

The yellow beeswax, *cera flava* (B.P.), is known as *ghedda* and *mom* in Hindustani. It is a secretion formed by the bee, *Apis mellifica* Linn., and possibly also by other species of bees and is used by the insects to construct the cells of the honeycomb. The wax is produced in the form of scales from the rings of the abdomen of bees. Wax also exists in plants

bearing in this, as in other respects a close analogy to the fixed oils. A wax is also produced by the Indian *Kota bees*, belonging to the genus of *Melipona* (a minute stingless insect) and furnish a sticky, dark-coloured wax, resembling in physical character the propolis rather than true wax. After extraction of honey, the comb is melted in water, and as the impurities settle in the bottom of the vessel, the wax on top of water can be strained and run into moulds and cooled. One pound of pure beeswax can be obtained from 20 pounds of honeycomb. It is in form of a yellowish brown, solid and brittle mass and becomes plastic when warmed. Beeswax contains about 80 per cent myricin or myricyl palmitate, 15 per cent cerotic acid, aromatic body and possibly some melisic acid and stearate melting at 62° to 64°C.

It has been used for a long time in making candles and as earplugs to deafen noises. It is now used in paints, polishes, pillmass, plasters, ointments and in various other products of industries.

5. Pollens (bee bread)

Bee bread is a sort of paste prepared by the nurse bees with pollens principally mixed with a little honey and water. The grub during 3 to 5 days of its development is fed mainly on this food. Pollens are highly rich in natural vegetable proteins. Bee larvae live mostly on pollens during the first days of larval life. It has been shown that pollen-starved larvae do not become efficient honey collectors nor can they manufacture the right type of venom.

6. Honey (*mel depuratum*)

Honey is a saccharine secretion deposited in the honeycomb by the bees, *Apis mellifica* Linn., known as *modhu* in Hindi, Sanskrit and Bengali, *madhu* in Gujrati and Tamil and *shahad* and *makhyan* in Punjabi. The saccharine matter is extracted from the nectaries of flowers.

Nectar is a highly complex material containing considerable percentage of water, a few chemically different sugars, minerals, acids, colouring and flavouring materials and enzymes. The bulk of all sugars contained in the nectar consists only of cane sugar but small quantities of dextrose and levulose are also present. Bees extract this nectar from the nectaries of various flowers. This fluid is usually insipidly sweet. The composition of nectar varies in different plants. The composition and the flavour of honey will vary accordingly. The honey made from nectar collected from poisonous flowers as mountain laurels, yellow jessamine and jimson weed, etc., may be quite toxic and hypnotic in nature. The honey made from nectars of lotus, fruit and clove and blossom is highly esteemed in flavour and use.

The nectar, when collected by the bees into their 'honey-stomach', is pre-digested and chemically converted by the secretion of glands

* *Apicur* (Hoffman La-Roche, Switzerland); *Forapin* (Coats and Cooper, London); *Apicosan* (Chemische Fabrika Vincis, Bredfeld, Germany); *Immenin* (Sero-therapeutic Institute, Vienna); *British Bee Venom* (Antibody Products, London, etc.).

situated in the head and thorax into levulose and dextrose. The finest honey is the one which is allowed to drain off from the comb. The centrifuged honey is much cleaner and free from foreign substances such as parts of insects, leaves, pollen grains, etc. California, stated to be the largest producer of honey, makes the U.S.A. the greatest honey-producer in the world, the annual production being 100,000,000 to 169,000,000 lb.

Honey occurs in nature as viscous, translucent, thick syrupy liquid, or as a soft opaque crystalline semisolid mass varying in colour from white to reddish brown. Purified honey is a thick, translucent, pale yellow or yellowish brown liquid with characteristic taste.

Chemistry of honey.—The important constituents of honey are: water, small quantity of sucrose, dextrose, levulose, wax, protein, volatile oil, formic acid, pollens, etc. Pure hill honey contains 70 to 80 per cent of dextrose and levulose. Pure honey has a specific gravity of 1.359 to 1.361, optical rotation of a 20 per cent w/v decolorized solution from $+0.6^\circ$ to -2° , corresponding to a specific rotation of $+3^\circ$ to -10° for the original purified honey. Chopra (1936) reported the analysis of honey as: water 17.7 per cent, available sugar 74 per cent in form of sucrose, levulose and dextrose, protein (pollens) 0.1 per cent, carbohydrate 20.21 per cent, ash 0.2 per cent w/w, and absence of vitamins A, B and C. Mineral constituents of honey are calcium 0.004, phosphorus 0.019, iron and copper 2 per cent (Chopra, 1936). According to McCamac and Widowson, honey contains on the average: water 20 per cent, protein 0.3 to 0.6 per cent, carbohydrate 74.4 to 79.6 per cent, calories 319 to 307 per 100 gm., ash 0.2 per cent w/v, calcium 7.7 mg. per cent, total phosphorus 32.3 mg. per cent, total iron 0.2 mg. per cent, and riboflavin (vitamin B₂) 106.0 mg. per cent. These figures show that honey is rich in easily digestible sugars and has a high caloric value. It is also rich in iron and copper. The difference between honey and sugar solution being that honey contains pre-digested invert sugars such as dextrose and levulose which are easily assimilated by the system without undergoing further process of digestion, whereas sugar consists mostly of sucrose only and is lacking in the enzymes *invertase* and *diastase*.

Bactericidal properties of honey.—Prica (1938) reported that natural honey diluted 1 in 5 with tap water is highly bactericidal for Gram-positive and Gram-negative organisms. This bactericidal property is destroyed when honey is heated at 60° to 90°C . for a short time but it is not lost by neutralizing the acidity of honey or after a long exposure to diffuse daylight. Dold, Du and Dzio (1935) showed that the antibacterial substances, *inhibins*, in natural honey are effective against bacteria and not against moulds, fungi and yeast. The *inhibins*

are destroyed by heating honey for five minutes at 100°C ., 10 minutes at 80°C . and half an hour at 56°C . and one hour exposure to sunlight. The *inhibins* are retained in honey for months in absence of sunlight and sunheat. This property is lost after passing honey through Berkfeld filter and asbestos filter and is also adsorbed by kaolin and aluminium oxide.

Uses of honey.—Honey is a demulcent and a sweetening agent. There is a considerable list of sweetening and flavouring agents in the pharmacopœia such as cane sugar, glucose, glycerine, saccharine, chloroform, liquorice, honey and fruit syrups. All of these are used to disguise the obnoxious taste of medicine and to make the preparation more elegant in dispensing. Of all these agents honey is to be preferred as it is not only a sweetening agent but also a food. Honey is dispensed in pharmacopœia as *oxmel* (containing acetic acid and honey), *Oxymel scilla* (containing squill and honey) and *Mel rosa* (containing 25 per cent of fresh rose petals and honey). Honey is used as a demulcent, laxative and a nutrient food. During the present war emergency the author suggested that honey could be safely substituted as a vehicle and as a nutrient agent in place of glycerine.

The medicinal properties of honey have been known to our ancestors from the earliest times. That our ancestors were well acquainted with medicinal uses of honey is seen from the uses of honey mentioned in *Sushruta Samhita* and *Asthanga Hridayam*. These two classical publications from Ayurveda described in few slokas the medicinal values of honey. These works described the classification of bees in relation to their habits, medicinal value of honey and differences between pure and the heated honey. Honey has been used as a food for children as it is easily digestible sugar and acts as an intestinal disinfectant. Without any doubt honey should be given more attention in the problem of feeding of invalids and infants because next to milk it is best food for children. Two to three teaspoonfuls of honey given to children twice daily will result in an increase in weight and will also raise the hæmoglobin content of blood. Infants fed on honey rarely show any sign of flatulence. It is said that orange juice may be dispensed in children fed on honey. Schultz and Knott observed that infants of six months and over digested honey more rapidly than ordinary sugar during the first fifteen minutes of digestion. There was a greater average gain of weight per day. Honey is known to be the best healer of wounds and is superior to all ointments. Honey soothes pain, hastens healing and is highly effective in burns and carbuncles. Grundle and Blattner pointed out that honey played an important rôle in the art of healing during the middle ages. It is recommended for treatment of ulcerated wounds by the application of a piece of linen smeared with honey. It is recommended for inflamed wounds of mouth,

throat and digestive tract and fresh and bleeding wounds. The other uses of honey as for hiccup, antidote against poisons, for high blood pressure, leprosy, diabetes, intestinal worms, eye troubles, asthma, diarrhoea and vomiting, etc., have been mentioned.

Commercial and odd use of honey.—In the 'Believe It Or Not' leaflet on the propaganda on honey the American Bulletin of Honey, Madison, Wisconsin, U.S.A., the following commercial uses of honey are mentioned :

About 6,000,000 lb. of honey is used in different types of cookies in making bread, beverages, cakes, candies, fruit drops, sauces, meats, and fish preparations; pies, pudding, salads and other vegetable preparations. Honey is used in golf-balls to make them heavy and of the proper specific gravity. Honey is added to the chewing tobacco, chewing gums, cigarettes and babies' sucking teats. The smoking pipes are immersed in honey for some days to cure them. It is added to cosmetics, tooth-pastes and shaving creams. It is used to enhance the natural darkness of onyx and other stones used in jewellery. It is also used in weather-proofing of leather.

Summary and conclusion

Different aspects of bee farming industry in India have been discussed. The Indian farmers and agriculturists have not shown so far much keenness towards bee farming, the collection and sale of honey apparently due to the fact that collection and sale of honey in itself is not a paying proposition. With the exception of hills the plains do not provide a large number of nectar bearing perennial flowers, nor do the bees like to stay in the plains throughout the year. The bee farming industry, however, can be made more attractive and lucrative concern if efforts could be made to exploit the by-products of this industry. The therapeutic value of by-products of this industry as *bee milk* (royal jelly), *bee glue* (propolis), *bee bread* (pollens) and *bee venom*, has been discussed in the body of this paper. The therapeutic uses of bee venom in myalgias, neuritis, rheumatic endocarditis and choroiditis are well known and are established in medicine. Other interesting and curious properties as nutritive value of and the presence of female sex stimulating hormone in royal jelly, healing properties of propolis in sores and ulcers, and the bactericidal and the nutritive value of honey are also discussed. It is suggested that honey could easily replace glucose and glycerine particularly as a war emergency measure since honey possesses many more therapeutic properties in advantage over glucose. The bee farming industry is likely to become more attractive not only to agriculturists but to florists, fruit-culturists and to the medical profession, if all the features discussed above could be properly investigated and exploited.

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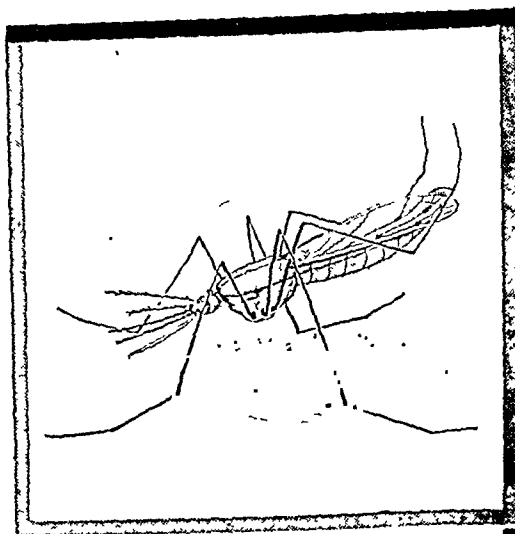
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Indian Medical Gazette

OCTOBER

THE VITAMINS, AND ASSOCIATED SUBSTANCES AND CONSIDERATIONS

THESE reagents in nutrition have been known to the medical profession in Europe since medieval times, as subtle principles existing in fresh food, not found in preserved food and affording protection against scurvy and similar diseases. The sailors were called 'limeys' because of their ration of lime juice. The physical status of the principles as substances was, however, established between 1897 and 1909, in connection with beri-beri in Asia. In 1911 the term *vitamine* (vit = life; amine which the substance was believed to be) was introduced in America. They were called *Accessory Food Factors* in England. In 1915 a distinction was made between the water soluble and fat soluble vitamins. So the study progressed. The individual vitamins A, B, C, D and others were not only recognized with certainty but also prepared synthetically. Now they are known as chemicals also. In future they will be known as chemicals only. To-day, 38 years after they were given a name, there are some 31 vitamins and provitamins (Beaumont and Dodds, 1947). The last well known member of the B group, B₁₂, was described only last year and folic acid was synthesized but three years ago.

Newer knowledge: (1) *Vitamin A*.—It is divisible definitely into A₁ and A₂, occurring typically in sea fish and river fish respectively. Both of them function in the retina and provide the photo-sensitive pigment, in addition to keeping the outer coats of the eye in good condition.

This vitamin does not appear to be anti-infective as was thought a few years ago (Topley, 1933). A hypervitaminosis is possible at least in children (Toomey and Morissette, 1947). It is characterized by 'soreness and swollen legs' caused by interference with the growth of epiphyses and periosteal thickening. Toxic symptoms due to ingestion of the liver of the polar bear by explorers of polar regions are also believed to be due to hypervitaminosis A.

Although the defect in dark adaptation (Harrow, 1946) and night-blindness (Micks, 1947) are the earliest recognizable symptoms of vitamin A deficiency, all night-blindness is not due to this cause. According to the Council of Pharmacy and Chemistry of the American Medical Association administration of vitamin A to drivers of automobiles will not diminish accidents at night (Harrow, *loc. cit.*).

(2) *Vitamin B*.—This is not a single substance but a group and has now 11 members: (i) *Thiamin*. It is heat-labile anti-neuritic factor. B₁ and aneurine are the other names. It is derived from natural sources (animal products, vegetables, fruits and seeds) or prepared by laboratory synthesis. It appears to be an essential link in the utilization of carbohydrates (Micks, *loc. cit.*), the specific action being on pyruvic acid which is ultimately broken down into CO₂ and H₂O. (ii) *Riboflavin*. It is fairly heat stable but very photo-labile and also known as B₂ or vitamin G. It can also be derived from natural sources or prepared by laboratory synthesis. Its deficiency is typically associated with buccal and ocular disorders and seborrhœic dermatoses. The symptoms of its deficiency are usually complicated by other factors. (iii) *Niacin*. Also known as *nicotinic acid*, *nicotinic acid amide* or *B. B. Factor*. It is the anti-pellagra vitamin. (Pellagra, incidentally, vies with syphilis in the richness of its symptomatology and the dissimilarity of ways in which it comes to the clinician—Spillane, 1947). Lately it has been used in syphilis also in allaying girdle pains in *tabes dorsalis* (Pelner, 1947; abstract this journal, April 1949, p. 172). (iv) *Pyridoxine*. Also called vitamin B₆. Deficiency of vitamin in rats causes a pellagra-like disease which cannot be cured with nicotinic acid. Acrodynia has been associated with the lack of this vitamin. The dermatitis resulting from pyridoxine deficiency can be cured by essential fatty acids (unsaturated fatty acids of the type of lanoleic acid). Alanine (α-amino-propionic acid) can also replace pyridoxine as a growth factor for *Streptococcus lactis*, suggesting that it may be a precursor of the vitamin. (v) *Pantothenic acid*. Deficiency of this substance in rats shows poor growth, dermatitis and greying of hair. The royal jelly, a liberal dose of which changes a female bee larva into the queen, is the richest known source of pantothenic acid. The acid thus converts to female coolie of the insect world into a queen. (vi) *Biotin*. Also known as *Anti-Egg-White Injury Factor*, *Vitamin H* and *Co-enzyme R*. Egg white as a source of protein in rat diet gives rise to a severe dermatitis because of its avidin content. Biotin neutralizes the avidin. Normal human beings eliminate a considerable quantity of biotin daily in a free state. Intestinal bacteria synthesize biotin readily. Avidin is an anti-vitamin and so may be many other substances. Biotin has a pro-carcinogenic effect, thus: (a) butter yellow gives rise to tumour of the liver in rats; (b) riboflavin protects against this danger; (c) biotin neutralizes this protective influence. (vii) *Para-aminobenzoic acid*. It is an essential growth factor in chicks and is also needed by rats for keeping their fur normal. It also prevents greying of rats and mice. Two other important reactions of the acid are: (a) specific action on the virus and toxæmia of scrub typhus (Editorial, 1949); (b) neutraliza-

tion of sulphanilamide, the two substances competing for the possession of an enzyme which renders the organism susceptible to the sulphone used. (viii) *Inositol*. It is the mouse anti-alopecia factor. (Thus 3 vitamins keep hair healthy and fully pigmented, at least in animals: pantothenic acid, para-aminobenzoic acid and inositol. Biotin has also been considered helpful.) The vitamin is synthesized by intestinal bacteria. (ix) *Choline*. Besides being a constituent of lecithin, etc., and playing a part in fat metabolism, this substance is also a vitamin. It prevents perosis (shortening and thickening of bones) in chicks and promotes growth in turkeys, chicks and dogs. It is also needed for lactation and growth of rats. (x) *Folic acid*. Originally obtained from green leaves (folium = leaf), this substance has been prepared synthetically and given a place in the treatment of anaemia, sprue, etc. (Editorial, 1946). (xi) *Vitamin B₁₂* is probably pteroyl-glutamic acid and occurs in crystalline form as small red needles. It is an outstanding discovery of the present century. It appears to succeed where folic acid failed after raising hopes and alleviates neurological complications in pernicious anaemia. Four tons of liver yield only 1 gm. of vitamin B₁₂, used in doses of 3 to 6 mg. (Berk *et al.*, 1948; British Medical Association, 1948; Editorial, 1948; Rickes *et al.*, 1948; Shrobb, 1948; West, 1948).

(3) *Vitamin C*.—It is ascorbic acid or cevantic acid. All animals except guinea-pigs and primates can synthesize it and the latter develop scurvy when deprived of it. In conditions arising from its deficiency there appears in the urine *p*-hydroxyphenyl-pyruvic acid. Diabetes is made worse by the deficiency.

Gluco-ascorbic acid, a substance structurally related to ascorbic acid, when fed to mice, produces in the animal a scurvy-like disease. The substance neutralizes the naturally existing ascorbic acid as para-aminobenzoic acid neutralizes sulphanilamide.

(Associated with this vitamin is another which is not anti-scorbutic and protects guinea-pigs from pneumonia. It has been called *Vitamin C₂* or *J* and is probably identical with 'grass-juice factor'.)

(4) *Vitamin P*.—It is derived from the lemon peel and is therefore also called *citrin*. It controls vascular permeability (hence the name, P). It appears to be related to hesperidine, a flavone derivative which also controls hæmorrhage by decreasing capillary fragility and occurs in the lemon peel.

(5) *Vitamin D*.—It controls the proper utilization of calcium and phosphorus and consists of about 10 substances. Of these 3 are now well known: (i) Vitamin D of the cod liver oil (also of the halibut liver oil, tunny liver oil, sword fish liver oil, in fact of the liver oil of all

fat fishes). It is found in the flesh of all fat fishes also. (ii) D₂. It is the ultra-violet irradiated ergosterol, also called *calciferol* and *viosterol* when dissolved in oil. (iii) D₃. It is irradiated 7-dihydrocholesterol. This cholesterol is present in animal fat and becomes activated naturally when the animals are exposed to sunlight. Probably provitamin and vitamin D in higher animals are derived from cholesterol and not from ergosterol. It is found in the tunny fish oil. The deficiency of vitamin D produces rickets and allied conditions. The vitamin has also been used in treating infantile tetany which is caused by a low calcium content of the blood. The vitamin works best in company with parathyroid hormone and is absorbed from the intestine in the presence of bile. Hypervitaminosis is possible.

(6) *Vitamin E*.—It is tochoferol (tocho = child birth; phero = bear; ol = alcohol). Like vitamins A and D it is soluble in fat and insoluble in water and also like them it occurs in the non-saponifiable fraction of fats and oils. Wheat germ oil is the richest natural source containing α -tochoferol and β -tochoferol. The α -form is the more active of the two and available as a synthetic product.

As implied in the name the vitamin influences the reproductive organs. It is also concerned in the functions of the muscular and vascular systems. Hopes raised in curing sterility, threatened abortion and muscular dystrophy have not yet been fulfilled.

(7) *Vitamin K*.—This is the 'koagulation' vitamin, a naphthoquinone. It occurs in 2 forms: K₁ and K₂. The former is obtained typically from alfalfa (lucerne, a fodder-like clover of the family *Leguminosæ*), and the latter from putrefied fish meal. The intestinal flora which putrefies food also manufactures vitamin K.

The vitamin helps in coagulation of blood by assisting in the formation of prothrombin in the liver.

In experimental work on rat the synthesis of the vitamin in the intestine can be prevented by giving sulphaguanidine which interferes with the nutrition of bacteria.

In the body the action of the vitamin is prevented by giving dicoumarol, an active principle obtained from sweet clover. The principle inhibits the production of prothrombin. Heparin acts similarly.

(8) *Vitamin T*.—The existence of this vitamin which increases the red platelets in rat and man is suspected. It may be a part of vitamin A. In function, however, it must be associated with vitamin K. Sesame oil is very rich in it.

(9) *Vitamin L*.—The existence of this vitamin is also suspected. It consists of L₁ (prepared from beef liver) and L₂ (prepared from yeast)

and assists in the maturation of lactation tissue (hence the name). They are 'filtrate factors' as opposed to the 'adsorbate factors', being found in the filtrate of the liver or the yeast preparation after the other factors have been removed by adsorption with Fuller's earth (Stephens, 1947).

(10) *Vitamin M*.—This vitamin, lack of which produces monkey pellagra in the familiar Indian brown monkey (*Macacus rhesus* of the Rh fame), may be only folic acid or a very closely associated substance.

(11) *Vitamin W*.—It may be vitamin B_w which is believed to be identical with biotin.

Detection and assay of vitamin.—As long as the animal test was the sole means of detecting the absence or presence of a vitamin, the latter remained confined to a few letters of the alphabet. Colour tests, spectroscopic tests and effects on the growth of bacteria have changed the situation rapidly and steadily within the last twenty years.

Avitaminosis.—In a normal human subject living a natural life and eating what he likes avitaminosis does not occur. Alcoholics and drug addicts who ignore their usual food, patients who are on special diets, prisoners of war during extensive campaigns, greedy coolies who come to towns from the countryside to gather gold at any cost and subjects dieting themselves for the purpose of slimming, are only liable. The poor village population of Northern India, as seen in recruiting soldiers and labourers, suffers only from lack of proximate principles and thrives on the military ration. Signs of avitaminosis often seen in the poverty-stricken town riff-raff, also examined for recruiting, are hardly ever seen in it, if pellagra be excluded. Of vegetable and fruit of some kind or other there is no dearth in Northern India countryside at all. Most of these vegetables and fruits are not marketable. If they could be brought and sold to the coolie at a special rate avitaminosis in the town labour, now seen, would cease. Morbidity and mortality in the town labour, incidentally, is caused more by discomfort and insanitation than any other aetiological agent. The labourer dies of any disease that he can contact because of these two handicaps, not because of avitaminosis or even lack of nutrition. All the death in hospitals in Calcutta during the recrudescence of bubonic plague in 1947 were among the non-Bengali labour (Editorial, 1948).

All the vitamins have not been found to be necessary for all the animals so far.—An open mind on the topic, however, is desirable. With the newer methods of detection and assay more information is bound to become available. That herbivorous mammals, like goat and monkey, specially the males, never really stop growing and that herbivorous reptiles like

tortoise seldom die of old age are worth remembering. All flesh is grass and should be capable of remaining green like grass.

Vitamins in plants.—Although all the vitamins are made in plants little is known of their rôle in plant physiology. In the plants they may be hormones (for the plant), sheer waste products or products which in natural selection have been found protective for the plant because of their distastefulness to the animals.

A link between vitamins and hormones in animals.—This is provided by cholesterol which is capable of forming vitamin D and also steroids of the hormones of the testes and ovaries. Dihydrotachysterol prepared from tachysterol which is an irradiation product of ergosterol has properties intermediate between those of vitamin D and parathyroid hormone (Cameron, 1947).

Trace elements in metabolism.—As opposed to the 'bulk substances' these substances act almost like vitamins and hormones. Many metals and non-metals act in this way besides acting as bulk substances. Ca so acting controls nerve function. The pharmacological action on the system of the minute quantities of the trace elements taken is not, however, the one commonly relied upon in allopathic medicine.

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Medical News

200TH ANNIVERSARY OF DR. EDWARD JENNER

(Reproduced from *Current Science*, Vol. 18, No. 6, June 1949, page 227)

To commemorate the 200th anniversary of the birth of Dr. Edward Jenner, the British physician, who introduced to the world the technique of vaccination, an exhibition has been arranged in London.

It was in 1798 that Dr. Jenner first placed before the world the results of his researches into the possibilities of vaccination. This new technique soon spread to all parts of the civilized world and by 1800 had become recognized medical practice. He was the first person to introduce the idea, and the first to have the courage to test his theories in practice.

It was about 80 years later that Pasteur extended Jenner's discovery by using vaccination against cholera and anthrax. It was he who proposed a meeting of the Medical Congress in London, that vaccination be officially adopted as the term for this method of conferring immunity from infectious diseases. He suggested this as a 'homage to the merit and immense services rendered to medicine by one of England's greatest men, Dr. Jenner'.

CENTRE FOR INTERNATIONAL CO-OPERATION IN LONDON

THE CIBA FOUNDATION

(Abstracted from the *British Medical Journal*, Saturday, 2nd July, 1949, page 27)

THE Ciba Foundation for 'the promotion of international co-operation in medical and chemical research' was opened on 22nd June, at 41, Portland Place, London, W.1, by Sir Henry Dale, O.M., F.R.S. The foundation has been endowed by the firm of Ciba, manufacturing chemists of Basle. The Centre will be used as a meeting place for medical research workers and clinicians, and there is accommodation for 15 visitors.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

(Reproduced from *The Medical Officer*, No. 2140 (Vol. : LXXXII, No. 5), Saturday, 30th July, 1949, page 411)

SIR CECIL WAKELEY, K.B.E., C.B., F.R.C.S., F.R.A.C.S., F.A.C.S., has been elected President of the Royal College of Surgeons of England in succession to Lord Webb-Johnson, President since 1941. Sir Harry Platt (Manchester) and Professor E. F. Finch (Sheffield) have been elected Vice-Presidents of the College.

INDIA : FIRST PHARMACY COUNCIL

(Reproduced from *The Pharmaceutical Journal*, No. 4468, Vol. 162, 4th Series, Vol. 108, Saturday, 18th June, 1949, page 453)

THE first Pharmacy Council of India under the Pharmacy Act, 1948, has been set up. This Council has been made quite broad-based with 34 members; 6 elected by the Inter-University Board, 6 nominated by the Central Government, one elected by the Medical Council of India, 3 ex-officio members, with 18 members nominated by the Provincial Governments. The first meeting of the Council was held in the Legislative Buildings, New Delhi, on 16th May last and was opened by the Minister for Health (Rajkumari Amrit Kaur). Thereafter, the business was conducted by the ex-officio chairman of the Council, the Director-General of Health Services (Dr. K. C. K. E. Raja).

At this meeting Professor M. L. Schroff, Editor of *The Indian Pharmacist* and now Principal, Birla Colleges, Pilani, Jaipur, was elected Vice-President. An Executive Committee of five was later elected: Mr. P. M. Nabar, Secretary, Drugs Technical Advisory Board and Chief Advisory Chemist to the Director-General of Health Services, Professor P. Srivastava, of the Benares Hindu University, Dr. B. Mukerji, Director, Central Drugs Laboratory, Dr. H. R. Nanji and Mr. B. V. Patel of Bombay. A sub-committee of seven to prepare uniform educational regulations under Section 10 of the Pharmacy Act was also appointed.

ADVERSE EFFECT OF MIXING TAPIOCA AND SWEET POTATOES IN WHEAT FLOUR

(Extracted from *Current Science*, Vol. 18, No. 8, August 1949, page 294)

MR. P. N. AGARWAL writes :—

For overcoming the food shortage in the country, the Ministry of Food has recommended the mixing of tapioca and sweet potatoes meal in wheat flour. This scheme, while calculated to increase of food supply of the country, is likely to produce an adverse effect on the health of the nation, which is already suffering from an ill-balanced diet.

Both tapioca and sweet potatoes are rich in carbohydrates which is principally starch. The addition of these starchy foods to wheat flour would render it ill-balanced. The resulting mixture will have less protein and fat and much more carbohydrate. These changes in protein, fat and carbohydrate contents will be proportional to the quantity of tapioca or sweet potatoes incorporated. Thus though the calorie intake of food will be increased due to the added carbohydrate there will be a marked fall in the percentage of the protein, and is likely to be a more widespread incidence of the deficiency diseases in the country.

DIRECTOR OF ARMY HEALTH

(Reproduced from the *British Medical Journal*, 7th May, 1949, page 829)

THE title of Director of Hygiene at the War Office has been changed to Director of Army Health. The titles of Deputy Directors, Assistant Directors, and Deputy Assistant Directors have been changed similarly. Specialists in Hygiene are now entitled Specialists in Army Health.

RATIO OF DOCTORS TO POPULATION

(Reproduced from the *Lancet*, 28th May, 1949, page 940)

A DRAFT report on the medical professions in 23 countries, published last year in New York by the

World Medical Association, records the ratio of doctors to population in various parts of the world. These figures were printed in the *Journal of the American Medical Association* of 1st January (page 38) and include the following:—

Country	Population	Doctors	Doctors per 100,000 population	Population per doctor
U.S.A. ..	141,228,673	197,605	140	710
Great Britain ..	48,788,000	55,771	114	870
Denmark ..	4,044,725	4,250	105	950
Canada ..	11,489,713	11,901	104	970
New Zealand ..	1,750,000	1,800	103	970
Australia ..	7,500,000	7,137	95	1,100
Switzerland ..	4,000,000	3,806	95	1,100
Sweden ..	6,700,000	6,360	95	1,100
Spain ..	27,000,000	25,142	93	1,100
Norway ..	3,126,000	2,900	93	1,100
Netherlands ..	9,000,000	8,000	89	1,100
Czechoslovakia ..	12,000,000	9,300	78	1,300
France ..	40,000,000	30,000	75	1,300
Eire ..	3,000,000	2,000	67	1,500
South Africa ..	11,391,949	4,800	42	2,400
China ..	450,000,000	20,000	4	25,000

JOURNAL OF DUTCH AND INDONESIAN TROPICAL MEDICINE

(Reproduced from the *Lancet*, 28th May, 1949, page 940)

RECOGNIZING that medical articles published in Dutch are intelligible to a comparatively small number of readers, and that the mother tongue of Indonesia—the Bahasa Indonesia—is still more restricted, a foundation with headquarters in Amsterdam has launched a new quarterly journal of tropical medicine in English—*Documenta Neerlandica et Indonesica de Morbis Tropicis*. The editors hope that much of the work done in Surinam and the Netherlands Antilles, as well as in Indonesia, will eventually be recorded in the *Documenta*. The annual subscription is £1 2s. 6d., payable to F.K.A.A., Lambrecht, 268, Rivierenlaan, Amsterdam 7, Netherlands.

ROYAL COLLEGE OF NURSING: ATTEMPTED SUICIDE AND THE LAW

(Reproduced from the *Medical Press*, 17th August, 1949, page 154)

A COMBINED resolution in the names of the Royal College of Nursing and the Association of Hospital Matrons for consideration at their Representative Council meeting in October will be to the effect that the law be amended so that attempted suicide is no longer regarded as a crime. Matrons and sisters feel strongly that their task of nursing these cases, who are often so gravely ill, of infusing in them the courage to face life once more is seriously impeded by the presence of a police officer, however kindly, and all the other police measures the law demands.

DEATH FROM PENICILLIN

[Reproduced from the *Medical Review*, Vol. XLIII, No. 6, June 1949 (Series No. 513), page 80]

THE death is recorded by Dr. George L. Waldbott (*J. Amer. Med. Assoc.*, 19th February, 1949) of a woman,

aged 39, who had had two courses of penicillin previously for what appears to have been attacks of asthma. She was again treated with penicillin. Within five seconds after injecting 50,000 units she complained of a strange taste in the mouth and tongue and of swelling and tightness in the throat and nose. Her face became flushed, bloated, and extremely cyanotic, and she felt itchy all over. Leaning forward over a table and asking for a glass of water, she suddenly collapsed and died immediately. The cause of death is stated to have been anaphylactic shock. It is thought that the injection must have been given intravenously through accidental puncture of a vein. This was indicated by the appearance of blood at the site of injection and by the strange taste in the mouth, which is so characteristic in intravenous therapy and is regarded as an ominous sign by those who have constantly to deal with allergic patients. The lesson we learn from this case is that the greatest care should be exercised in the administration of any of the newer remedies if we are to avoid disastrous occurrences.

A NEW SURGICAL JOURNAL

THE *Dutch Archives of Surgery* is the new official organ of the Dutch College for the advancement of surgical science. It will appear quarterly and each issue will contain about 80 pages of which 16 will be devoted to illustrations. It is published in English because of the desire of Dutch surgeons to make their contributions available outside Holland and to take their place in the international science of surgery. The papers in the first issue of the journal are of high order and are well-printed and illustrated. The subscription rate is £2-2-0 per annum and the agents are Messrs. Baillière, Tindall and Cox, 7 and 8, Henrietta Street, London, E.C.2.

CLEARING HOUSE ACTIVITIES OF UNESCO FOR PERIODICAL REPRODUCTION

UNESCO was instructed by the Third Session of the General Conference held in 1948 to devise a means for the reproduction of out-of-print periodicals. A small number of periodicals in the fields of higher studies and advanced technology was selected and enquiries were made of their publishers whether they were out of print.

Contact was made with publishing groups and individuals in Canada, France, Germany, the Middle East, the United Kingdom, and the United States, where work has already started on the reproduction of out-of-print periodicals. In order to further the work being carried on in different countries, Clearing House activities for periodical reproduction have been established in connection with the general publication clearing house activities of the UNESCO Libraries Division.

Reports and enquiries received about out-of-print periodicals are centralized in the clearing house, and an attempt will be made to publish from time to time reports on the progress of work now being done in periodical reproduction. Particularly important in this respect is the development of union catalogues in various countries of long runs of periodicals on microfilm. The Committee on reproduction of periodicals of the Association of the Research Libraries of the United States has been most active in ascertaining the demand for the reproduction of United States periodicals.

For the present, attention will be directed to the reproduction of out-of-print issues of the following periodicals: *Nature*, *Architectural review*, *The economist*, *Revue générale des sciences pures et appliquées*, *Journal of experimental medicine*, *Journal of biological chemistry* and *Review of economic statistics*. All these publications are in demand from libraries throughout the world and all of them have issues from 1939 to 1945, and some preceding years, out-of-print.

Suitable methods will be employed to reproduce the number of copies required to meet the demand for subscriptions.

Libraries concerned to secure out-of-print issues of the above publications should write direct to the Libraries Division of UNESCO, stating exactly which issues they need. At least 100 subscriptions must be received before any individual issue can be reproduced by photo-lithography. It is estimated that the demand will be sufficient to permit the use of only for out-of-print issues from 1939. . . . price of each issue will be the same as originally set by the publisher. Issues out of print prior to 1939 will be considered for microfilming rather than for photo-lithography. The price of microfilm will be approximately $\frac{1}{2}$ cent. (U.S.) or 1.50 French francs a page.

Payment for reproduced issues may be made with UNESCO Book Coupons in those countries to which the Book Coupons have been made available.

Inquiries on the part of institutions which wish to have copies of the periodicals proposed for reproduction should be sent to UNESCO, Libraries Division, 19, Avenue Kleber, Paris 16.

Any contribution which can be made to the work of the Clearing House will be greatly appreciated.

STEPS TO MEET SHORTAGE OF MEDICAL SPECIALISTS

(Reprinted from the *Pakistan Medical Journal*, Vol. II, No. 5-6, May-June 1949, page 51)

A PRESS NOTE issued by the Ministry of Food, Agriculture and Health (Health Division), Government of Pakistan, says :—

To meet the shortage of high-grade medical specialists, the Government of Pakistan propose to recruit such of the following vital categories of staff from abroad as are not available in Pakistan :

Physicians :—Psychiatrist; Specialist in Heart Diseases; Specialist in Pædiatrics; Dermatologist, etc.

Surgeons :—Thoracic Surgeon; Plastic Surgeon; Ophthalmic; ENT Special; Gynæcologist.

Technicians :—Analytical Chemist; Biochemist; Pharmacist; Physiotherapist; Medical Writer; Blood Bank Technician.

Other Specialists :—Anaesthetist; Pathologist; Bacteriologist; Radiologist; Pharmacologist; Radio-therapeutist.

To ensure that local talent is not inadvertently overlooked, the Government are anxious to compile complete and accurate information regarding Pakistani Specialists in the above-mentioned categories.

Doctors with research and teaching experience, including those already in service of the Central and Provincial Governments, who desire to be considered for employment in any of these types of appointments, are requested to furnish directly to Deputy Secretary, Ministry of Food, Agriculture and Health (Health Division), Government of Pakistan, Karachi, information regarding their age, qualifications and experience, present occupation and the minimum salary acceptable, (i) if private practice is allowed, (ii) if private practice is not allowed. This information is required before 4th June, 1949.

[Received late for publication.—EDITOR, I.M.G.]

AMENDMENTS TO DRUG RULES, 1948

COPY of Health Ministry's Notification No. F.18-3/46-D, dated the 7th October, 1949, to the Publisher, *Gazette of India*.

In exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendments shall be made in the Drug Rules, 1945, the same having been previously published as required by the said sections, namely :—

In the schedules annexed to the said rules :—

1. In Schedule D after item 4, the following item shall be inserted, namely :—

'5. Medicines prepared in accordance with and intended solely for the treatment of patients under the Homœopathic system of medicine. All the provisions of Chapter III of the Act and the Rules thereunder subject to the condition that a container containing such drugs shall bear a label "Homœopathic Medicine".'

2. In Schedule K after item 7, the following item shall be inserted, namely :—

'8. Medicines prepared in accordance with and intended solely for the treatment of patients under the Homœopathic system of medicine. All the provisions of Chapter IV of the Act and the Rules thereunder subject to the condition that a container containing such drugs shall bear a label "Homœopathic Medicine".'

Copy of Notification No. F.1-42/47-D, Government of India, Ministry of Health, dated New Delhi, the 7th October, 1949.

NOTIFICATION

The following draft of a further amendment to the Drug Rules, 1945, which it is proposed to make in exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), is published as required by the said sections for the information of all persons likely to be affected thereby and notice is hereby given that the draft will be taken into consideration on or after the 15th January, 1950. Any objections or suggestions which may be received from any person with respect to the said draft before the date specified will be considered by the Central Government.

DRAFT AMENDMENT

In Schedule F appended to the said rules, in Part XII, under the heading 'D-Preparations containing any vitamins in a form not to be administered parenterally', in the sub-head relating to *Labelling* for the entry No. 1, the following shall be substituted, namely :—

'1. The number of units and/or the actual weight of each vitamin per unit volume and/or weight shall be declared on the label.'

(Sd.) J. N. SAKSENA,
Under Secretary.

Copy of Notification No. F.7-7/49-DS, dated the 7th October, 1949, from the Government of India, Ministry of Health, New Delhi.

NOTIFICATION

In exercise of the powers conferred by section 14 of the Pharmacy Act, 1948 (VIII of 1948), the Pharmacy Council of India is pleased to declare the following qualifications to be approved qualifications for the purpose of qualifying for registration as Pharmacists under the said Act, namely :—

- (1) the degrees in Pharmacy obtained from any of the accredited colleges of Pharmacy of the United States of America as issued by the American Council of Pharmaceutical Education from time to time;
- (2) the degree of B.Pharm. or B.Sc. (Pharm.) of a British University;

- (3) Diplomas of Chemist and Druggist and Pharmaceutical Chemist of the Pharmaceutical Society of Great Britain.

(Sd.) K. C. K. E. RAJA,
President,
Pharmacy Council of India.
(Sd.) J. N. SAKSENA,
Under Secretary.

Copy of Notification No. F.1-7/48-D, Government of India, Ministry of Health, dated New Delhi, the 7th October, 1949.

NOTIFICATION

The following draft of certain further amendments to the Drug Rules, 1945, which it is proposed to make in exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), is published as required by the said sections for the information of all persons likely to be affected thereby and notice is hereby given that the draft will be taken into consideration on or after the 15th January, 1950. Any objections or suggestions which may be received from any person with respect to the said draft before the date specified will be considered by the Central Government.

DRAFT AMENDMENTS

In Schedule C(1) to the said rules, for items 1, 3, 5, 6 and 7, the following items shall be substituted, respectively, namely :—

- '1. Drugs belonging to the Digitalis group and the preparations thereof not in a form to be administered parenterally';
- '3. Adrenaline and the preparations thereof not in a form to be administered parenterally';
- '5. Vitamins and the preparations thereof not in a form to be administered parenterally';
- '6. Liver extract and the preparations thereof not in a form to be administered parenterally'; and
- '7. Hormones and the preparations thereof not in a form to be administered parenterally.'

(Sd.) J. N. SAKSENA,
Under Secretary.

Copy of Notification No. F.1-5/48-D, Government of India, Ministry of Health, dated New Delhi, the 7th October, 1949.

NOTIFICATION

The following draft of certain further amendments to the Drug Rules, 1945, which it is proposed to make in exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), is published as required by the said sections for the information of all persons likely to be affected thereby and notice is hereby given that the draft will be taken into consideration on or after the 15th January, 1950. Any objections or suggestions which may be received from any person with respect to the said draft before the date specified will be considered by the Central Government.

DRAFT AMENDMENTS

- I. In the said rules for Rule 106, the following rule shall be substituted, namely :—

—'106. Diseases which a drug may not purport to prevent or cure.

No drug may purport or claim to prevent or to cure one or more of the diseases or ailments specified in Schedule J or to procure or assist to procure miscarriage in women.'

- II. For the heading to Schedule J annexed to the said rules, the following heading shall be substituted, namely :—

'Diseases and ailments (by whatever name described) which a drug may not purport to prevent or cure.'

(Sd.) J. N. SAKSENA,
Under Secretary.

Copy of Notification No. F.1-19/48-D, Government of India, Ministry of Health, dated New Delhi, the 10th October, 1949.

NOTIFICATION

The following draft of a further amendment to the Drug Rules, 1945, which it is proposed to make in exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), is published as required by the said sections for the information of all persons likely to be affected thereby and notice is hereby given that the draft will be taken into consideration on or after the 15th January, 1950.

Any objections or suggestions which may be received from any person with respect to the said draft before the date specified will be considered by the Central Government.

DRAFT AMENDMENT

In Schedule A to the said rules, in Form 21 under the heading 'Conditions of licence' after Condition 3, the following shall be inserted, namely :—

'4. If the licensee wants to sell, stock, exhibit for sale or distribute, during the currency of the licence, additional products specified in Schedule "C" not included above, he should apply to the Licensing Authority for the necessary permission. This licence will be deemed to extend to the products in respect of which such permission is given. This permission should be endorsed on the licence by the Licensing Authority.'

(Sd.) J. N. SAKSENA,
Under Secretary.

Copy of Notification No. F.1-48/47D, dated the 12th October, 1949, from Government of India, Ministry of Health, to the Publisher, *Gazette of India*, New Delhi.

In exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendments shall be made in the Drug Rules, 1945, the same having been previously published as required by the said sections, namely :—

In the said rules :—

- I. Rule 24 shall be renumbered as sub-rule (1) of that rule and after sub-rule (1) as so renumbered, the following sub-rule shall be inserted, namely :—

'(2) A fee of rupees two shall be paid for a duplicate copy of a licence issued under this rule, if the original is defaced, damaged or lost.'

- II. In Rule 59, after sub-rule (2), the following sub-rule shall be inserted, namely :—

'(3) A fee of rupees two shall be paid for a duplicate copy of a licence issued under this rule, if the original is defaced, damaged or lost.'

- III. Rule 69 shall be renumbered as sub-rule (1) of that rule and after sub-rule (1) as so renumbered, the following sub-rule shall be inserted, namely :—

'(2) A fee of rupees five shall be paid for a duplicate copy of a licence issued under this rule, if the original is defaced, damaged or lost.'

IV. Rule 75 shall be renumbered as sub-rule (1) of that rule and after sub-rule (1) as so renumbered, the following sub-rule shall be inserted, namely :—

(2) A fee of rupees five shall be paid for a duplicate copy of a licence issued under this rule, if the original is defaced, damaged or lost.

V. In sub-rule (1) of Rule 124 for the words 'The United States Pharmacopœia' the words and figures 'Indian Pharmacopœial List, 1946, the United States Pharmacopœia' shall be substituted.

Copy of Notification No. F.1-19/48-D, Government of India, Ministry of Health, New Delhi, the 26th October, 1949.

NOTIFICATION

In exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendments shall be made in the Drug Rules, 1945, the same having been previously published as required by the said sections, namely :—

A. In the said rules :—

Rule 25 shall be renumbered as sub-rule (1) of that rule and after sub-rule (1) as so renumbered, the following sub-rule shall be added, namely :—

(2) The licensing authority may make an endorsement on the original import licence to include new items subsequently manufactured by the same manufacturer and imported by the same importer subject to the condition that an application is made on the appropriate form to cover such items and the prescribed fee deposited.

B. In the schedules annexed to the said rules :—

I. In Schedule A—

(1) In Form 8, for the word 'substances' the word 'drugs' shall be substituted and for the words 'Homes of drugs or classes of drugs' the words 'Names of drugs and classes of drugs' shall respectively be substituted.

(2) In Form 9, for the words 'substances', 'substance' and 'List of substances' the words 'drugs', 'drug' and 'names of drugs and classes of drugs' shall respectively be substituted.

(3) In Form 10—

(i) for the words 'substances' and 'names of drugs or classes of drugs' to which the licence applies the words 'drugs' and 'names of drugs and classes of drugs' to which the licence applies shall respectively be substituted.

(ii) at the end of para. 1, the following shall be added, namely :—
'and any other drugs manufactured by as may from time to time be endorsed on this licence'.

(4) In Form 12, for the words 'Names of drugs' the words 'Names of drugs and classes of drugs' shall be substituted.

(Sd.) J. N. SAKSENA,
Under Secretary.

AFGHAN GOVERNMENT TO LAUNCH ANTI-TYPHUS CAMPAIGN

(Reproduced from Press Release No. 150, dated 16th September, 1949, of the United Nations Information Centre Theatre Communication Building, New Delhi)

REGULAR outbreaks of louse-borne typhus occurring every year in Afghanistan, especially during the cold months, are attributable mainly to general insanitary living conditions and to overcrowding in homes, lodging

houses, schools, barracks, motor buses, and jails, according to Dr. R. L. Tuli, Medical Officer for the S.E. Asia Regional Office of the World Health Organization, just returned to Delhi after three weeks spent advising the Afghan Government and demonstrating anti-typhus control methods. 'In Afghanistan where there are only about 100 qualified doctors for a population of 12 million', Dr. Tuli reports, 'notification of typhus cases has hitherto not been compulsory, and the only figures available are of cases which have come to the notice of Medical Officers working at Government Dispensaries'.

The anti-typhus campaign in Afghanistan, Dr. Tuli recommends, should include the following measures :—

- (i) Prompt notification of all new cases.
- (ii) Building up reserve stocks of vaccine, D.D.T. insecticide powder, and dust guns.
- (iii) Issuing official instructions on typhus prevention to all doctors, Government Departments, and jail doctors.
- (iv) Instituting control measures in houses and other places where
- (v) Training of D.D.T. squads, and their posting at points of congregation (schools, bus stops, hospitals, waiting rooms, etc.).
- (vi) Instruction in all schools on dangers of lice.
- (vii) Nation-wide propaganda programme.

In putting the above measures into effect the Afghan Health Services will have the assistance of Mr. P. O. David, W.H.O. Sanitary Engineer, who will remain in Afghanistan for a further three months. Supplies of typhus vaccine and D.D.T. have already been procured for Afghanistan by W.H.O.

INTERNATIONAL HEALTH PROGRAMMES IN S.E. ASIA. W.H.O. REGIONAL COMMITTEE TO MEET NEXT WEEK

(Reproduced from World Health Organization, Press Release No. 151, dated 16th September, 1949, issued by United Nations Information Centre Theatre Communication Building, New Delhi)

Decisions of vital importance for the health of their peoples will be taken by representatives of Afghanistan, Burma, Ceylon, India, Thailand, France (French India) and Portugal (Portuguese India) attending the Second Meeting of the Regional Committee for S.E. Asia of the World Health Organization which will begin on 26th September* in New Delhi, announces the W.H.O. Regional Office. Dr. Martha Eliot, Assistant Director-General of W.H.O., will fly from Geneva for the meeting. Since last October, when at its First Meeting the Committee formally constituted the S.E. Asia Regional Organization of W.H.O., a Regional Office has been organized and has already provided disease-control demonstration teams, health surveys, fellowships, specialist advisers and other expert assistance to member Governments.

The Committee's tasks

The principal business of the meeting will be to review current W.H.O. activities in the Region and to plan the implementation in S.E. Asia of the W.H.O. programme for 1950 within the broad outlines decided upon by the World Health Assembly in Rome last June. Other agenda items are :—

Technical assistance to Governments in the preparation of antibiotics and other essential supplies.

Improvement of research and strengthening of teaching institutions.

[* Received late for publication.—Editor, I.M.G.]

Establishment of a Committee on health education in schools.

Conditions of service of public health personnel.

Mutual aid programmes for S.E. Asian countries.

Consideration of reports from Member States on nutrition, housing, etc.

Accommodation for regional office and staff.

A year's health progress

Progress reports will be heard by the Committee on six disease-control demonstrations at present being carried on in the Region by W.H.O. teams led by international experts. In India three malaria teams, using the most recent techniques of residual insecticide spraying, are operating in 250-sq.-mile areas in Terai (U.P.), Jeypore Hills (Orissa) and Malnad (Mysore), a fourth will shortly begin work in Wynad (Madras).

In the malarious regions of Chiangmai (Thailand) and Laghman (Afghanistan) two more malaria demonstration teams are already hard at work.

A venereal disease team is introducing modern control methods based on intensive penicillin therapy in the Himachal Pradesh (India) where venereal infections are a long-standing health problem of formidable proportions.

A Maternal and Child Health demonstration team will come to India later in the year. The U.N. International Children's Emergency Fund (U.N.I.C.E.F.) is providing supplies for four out of the six teams.

The value of the W.H.O. demonstration teams is not limited to the time and place where they actually operate. Training is given to parallel teams provided by national health services which can later extend operations into new areas. Attached to all W.H.O. teams are specially qualified public health nurses, who by house-to-house visiting and health education, seek to raise hygiene standards in the villages.

Among the other activities of W.H.O. of which the Committee will learn are the following:—

W.H.O. has awarded 43 Fellowships to give advanced training abroad to S.E. Asian public health workers.

An expert adviser has flown with supplies of vaccine and D.D.T. insecticide powder to assist the Afghan Government in launching an anti-typhus campaign. Twenty 'iron lungs' have been procured at short notice from the U.S.A. to help the Indian Health Services to combat the poliomyelitis menace.

W.H.O. is associated with the anti-tuberculosis campaign being carried out in Ceylon and India by U.N.I.C.E.F. and the Scandinavian Red Cross. Up to 1st September a total of 230,000 children and young people have been tuberculin tested, and 72,500 of them showing negative reactions have been protected against tuberculosis infection by vaccination with B.C.G. vaccine produced at the King Institute, Madras.

Finally W.H.O. experts, carrying out surveys on malaria situations in Afghanistan and Thailand, on venereal diseases in Simla (North India) and Afghanistan, and on filariasis in Ceylon, have made important recommendations concerning methods of attack on these diseases which will be examined by the Regional Committee.

Programme for 1950

A total 'regular' budget of seven and a half million dollars for 1950 was approved by the Second World Health Assembly meeting in Rome last June. A 'supplemental' budget of ten million dollars, depending on voluntary contributions from Member States, was also voted.

'The amount which may be allocated from the total W.H.O. budget for programmes in S.E. Asia', states the Regional Director, 'will depend in no small measure on the efforts made by individual countries of the region to derive the maximum benefit from the demonstrations and staff-training opportunities offered,

and on their acceptance of the obligations subsequently to carry on and expand the projects initiated by W.H.O.'

According to estimates which he will submit to the Committee, it may be possible in 1950, not only to extend the scope of 1949 projects in the region, but also to put new demonstration teams into the field; to launch control programmes in selected areas against plague, cholera, typhus and yaws; to carry out additional expert surveys of crucial regional health problems; and to provide regional Member States with the expert advice and assistance they may ask for to combat leprosy and to improve services in public health, mother and child health, health education or nutrition.

The recommendations of the Regional Committee concerning the 1950 W.H.O. programme in S.E. Asia will go before the Fifth Meeting of the W.H.O. Executive Board in Geneva next January. The Committee's proposals for the 1951 programme and budget will be included in a world programme to be submitted to the Third World Health Assembly next May.

The South East Asia Regional Office, opened in January of this year, was the first of six regional offices planned by W.H.O. to give effect to its policy of decentralization. Another has since been opened in Alexandria for the Eastern Mediterranean, while the old-established Pan-American Sanitary Bureau in Washington is now acting as W.H.O. Regional Office for the Americas. Each is responsible for carrying out in its region the programmes decided upon by the World Health Assembly and the W.H.O. Executive Board.

Other regional offices are to be opened in the near future in Africa, the Western Pacific and Europe.

The following will attend next week's meeting of the S.E. Asia Regional Committee:—

AFGHANISTAN	..	Dr. Faqir Mohamed, General Director, Ministry of Public Health.
BURMA	..	Hon'ble U. Maung, Minister for Foreign Affairs.
CEYLON	..	Hon'ble S. W. R. D. Bandaranike, Minister of Health. Dr. W. O. Wickramasinghe, Director of M. and S. Services.
INDIA	..	Hon'ble Rajkumari Amrit Kaur, Minister of Health. Dr. K. C. K. E. Raja, Director-General of Health Services.
THAILAND	..	Dr. Svasti Daengsvang, Deputy Director, Public Health.
FRANCE (FRENCH INDIA).		Colonel Doctor Bigot.

Observers will be present from the Nepal Government, the Indian Red Cross, the United Nations Information Centre, and the following United Nations Agencies: Educational, Scientific and Cultural Organization, International Labour Organization, Food and Agriculture Organization, International Emergency Children's Fund.

The name of the delegate for Portuguese India has not yet been announced.

CANCER

'CHESS BOARD' TECHNIQUE OF USING X-RAYS
By TREVOR I. WILLIAMS

Deputy Editor of the Scientific Quarterly 'Endeavour'
(Reprinted from a Release issued by the British Information Services, New Delhi)

ALTHOUGH the battle against cancer is, unhappily, still far from won, the doctor's armoury now contains some

powerful weapons to which thousands of people owe their lives. Outstanding among these is x-ray treatment which, although by no means universally effective, can, in some cases—especially when the patient is wise enough to seek early advice—effect dramatic cures.

A new technique of using x-rays, which is a complete departure from all existing methods, has been devised by Dr. Benjamin Jolles at Northampton General Hospital. This technique promises to be a real advance in a method which has already achieved a great deal of success.

Underlying principle

To understand what the discovery really means, something must be said of the principle underlying all kinds of radiation treatment. Briefly it is this: malignant cells are often more sensitive to radiation than healthy ones, and consequently if the intensity of the radiation used is carefully chosen, it may be possible to destroy the malignant cells without doing permanent harm to the others.

In carrying out this treatment, ever since it was first developed nearly half-a-century ago, it has been assumed to be essential that the radiation should be applied evenly to the part of the body being treated. This fundamental assumption is now being challenged, and, putting theory into practice, tests have shown a real advantage in interrupted radiation administered systematically.

Cancer peculiarities

Cancer differs from almost all other diseases, in that the body itself can make little contribution to its conquest. Indeed, up to a point, the stronger and healthier the patient is, the better the malignant cells are nourished. This is very different from, for example, a dangerous infection by germs, for, if such a drug as penicillin kills most of the germs, the natural defences of the body are marshalled to deal with the remainder.

Nevertheless, it seems that even in cancer the healthy cells can contribute, to some extent, to the overthrow of abnormal ones, and it is on this assumption that the new treatment is based. The x-rays fall on to a lead 'chess board', in which alternate squares are cut out, before reaching the area to be treated. Consequently, only half of the area is exposed to the rays at one time, and important structures—which play a part in the ultimate healing process—are untouched.

After a series of treatments, the lead 'chess board' is replaced by another in which the solid parts in the first correspond to holes, and *vice versa*, and the treatment is continued. Thus, the areas already treated are not affected, and their recovery is not interfered with.

Encouraging results

In order to be sure that no part escapes the rays, it is necessary that the chess board screens be accurately made and positioned. This is done by carefully marking the positions of the screen and the centres of the holes in it, so that, if necessary, it can always be put accurately in place, even during the course of treatment lasting for several weeks.

The new method is designed for growths which are easily accessible, and the results so far reported have been very encouraging. The rate of healing is very rapid, and the total quantity of radiation used is smaller than with the methods now in general use. The last point is vitally important, for the margin between a curative dose and a dangerous one is, at best, rather small.

Although the principle of the new treatment is quite simple, to carry it out successfully needs close co-operation of a team of experts. The dose has to be carefully estimated and measured in conjunction with a skilled histologist, who follows the results of the treatment by microscopic examination. It can, therefore, be carried out only in hospitals with extensive laboratory facilities.

Programme of research

This research is part of a wide programme of research sponsored by the British Empire Cancer Campaign, which finances research into cancer problems in universities and hospitals throughout Britain. It is a striking illustration of the way in which even after many years a fresh point of view can lead to a new advance in a direction in which the limit seemed already to have been reached.

Over the whole terrible spread of cancer the gain is, perhaps, not dramatic, though its significance must clearly await wider experiment; but already it has brought relief to those who had suffered for years, and it seems clear that, in the future an increasing number of sufferers will benefit.

The seriousness of cancer is too great to allow of any exaggeration of results. The new 'chess board' technique is important only in certain types of cancer but, nevertheless, it is a definite step forward. The whole problem to be solved is too complicated to give any real hope that it will finally be solved by a single spectacular discovery; only a series of smaller steps such as this will take us to the final goal.

PORTABLE ATOMIC PLANT TO PRODUCE RADIO-ACTIVE ISOTOPES

USE IN HOSPITALS AND MEDICAL CENTRES

(Reprinted from Release No. B.F. 2140 issued by the British Information Services, New Delhi)

Tests are being carried out in Britain on a portable atomic plant which has been produced by scientists after three years of experiments and is designed for use in hospitals, medical centres and health research units. The first of its kind in the world, it has been described as a miniature atomic pile.

The apparatus, which is known as Aspatron, produces radio-active isotopes. These are atomic elements giving off radiations which are of great value in medical work and research. These isotopes remain active for periods ranging from eight hours to three weeks.

The equipment is easily transported since it weighs barely two cwts. It produces isotopes by using uranium in the form of a pure oxide. This is arranged inside the apparatus in a specially designed pattern within a double wall of metal packed with the material which increases the efficiency of atomic reaction. There is no danger from radiation since its range is limited and nullified by adequate safeguards.

Problem of Transport

Hitherto, hospitals and medical units in Britain have been supplied with the isotopes they require from the atomic piles at the Government research station. Transport difficulties and the short time during which they remain active have, however, created many problems. This new portable apparatus will overcome these handicaps and spread the benefits of atomic energy in medical research over a much wider field.

The manufacturers of Aspatron plan to start commercial production as soon as tests confirm its potentialities. The cost of each individual equipment is estimated at about £500 (Rs. 6,667).

HOMŒOPATHY: NINETY PER CENT OF HOMŒOPATHS QUACKS, NEED FOR EFFEC- TIVE STATE CONTROL, CENTRAL COUNCIL AND PROVINCIAL BOARDS TO BE SET UP

'The practice of homœopathy in India is at present in the hands of a vast number of practitioners without proper scientific training. As many as 90 per cent of

homœopathic practitioners may fall under this category', says the Report of the Homœopathic Enquiry Committee which has just been published.

The Report adds, 'Homœopathic institutions in the country are ill-equipped and they are not able to impart proper training. This is the reason why the country has been flooded by quacks'.

The Homœopathic Enquiry Committee was appointed by the Government of India last year to make a survey of the position of homœopathic practice in India, the report on the available facilities for training in and the place of homœopathy in relation to medicine in all its aspects and to regulate such training and on the desirability of State control of the practice of homœopathy and the manner of its control.

The Committee met eleven times at various places in India and took evidences from witnesses representing a wide range of interests concerned with the subject-matter of the enquiry. A comprehensive questionnaire was drawn up and widely circulated. They visited homœopathic centres, institutions and pharmacies all over the country.

From the figures supplied by various institutions, the Committee surmise that the number of homœopathic practitioners may be between 200,000 to 300,000 whereas those who have received some sort of institutional training may number only about 5,000.

Elimination of Quackery

The Committee are strongly of the opinion that no State should permit quacks and quackery to flourish and that steps should be taken to eliminate them and to devise suitable measures for the control of the practice of homœopathic medicine. The issue of undesirable advertisements and literature must also be controlled. The methods of preparation of homœopathic medicines in India, their testing and dispensing should similarly be controlled. Colourable imitations of preparations of the regular system of medicine should not be permitted to be used and necessary steps should be taken to ensure that no homœopathic medicines are prepared or sold which do not conform to the prescribed standard.

After surveying the position regarding training in and practice of homœopathy in the U.K., the U.S.A., Brazil and Mexico, the Committee conclude that homœopathy, as a system of medicine, has a recognized status in these countries but that those who desire to practise it must have registrable medical qualifications.

Homœopathic Institutions

Institutions which provide training in homœopathy fall under five categories, namely:—

- (1) Those which attempt to teach the basic, pre-clinical and clinical sciences, although their equipment is generally very meagre and falls short of the standard of a medical school.
- (2) Those where basic, preclinical and clinical sciences are to be taught in addition to homœopathy although there is no equipment for giving scientific training.
- (3) Those where no attempt is made to teach either the basic or the preclinical or the clinical sciences.
- (4) Those which have got class rooms and some charts but regular teaching is not provided.
- (5) Those which exist only in name, their activity being confined to selling of degrees either by correspondence course or even without it.

None of the existing institutions has got facilities for research.

The Committee recommend that only institutions coming under categories (1) and (2) above be allowed to continue on condition that they conform to the standard of personnel, equipment and training in homœopathy as may be laid down and the institutions coming under other categories should be abolished.

'Pure Homœopaths'

The Committee observe that homœopathy has everything in common with the regular system of medicine, except the mode of its approach in therapeutics and in the methods of immunization. There is general agreement amongst homœopaths that the study of homœopathy and its practice should be based on methods of science. There is, however, a section of practitioners who differ from this view and style themselves as 'pure homœopaths'. They believe in the subjective symptoms and not in the modern scientific methods of diagnosis and the causation of diseased condition. The pure school of homœopaths constitutes a danger to society, the Committee state.

Registration of Practitioners

The question of registration and control of the homœopathic system of medicine has been considered by certain Provincial Governments and States from time to time but the position varies from province to province. The Committee consider that legislation for the control of the practice of and training in homœopathy should aim at: (1) adequate provision for supervision and control of homœopathic educational institutions and hospitals; (2) registration of practitioners of the homœopathic system; and (3) control over homœopathic pharmaceutical laboratories and manufacturing concerns. They recommend that the following categories of homœopathic practitioners should be placed on a 'register':—(1) Registered medical practitioners who have taken to the practice of homœopathy; (2) Medical practitioners holding degrees from foreign countries which entitle them to practise medicine in the countries where such qualifications are obtained; (3) Those who have successfully gone through the four years' course of training in any one of the following four institutions: (i) The Calcutta Homœopathic Medical College and Hospital, Calcutta; (ii) The Durham Homœopathic Medical College and Hospital, Calcutta; (iii) The Pratap & Hering Homœopathic Medical College and Hospital, Calcutta; (iv) The Bengal Allen Homœopathic Medical College and Hospital, Calcutta; and (4) Graduates of the Central College of Homœopathy, Calcutta, of the Regular College of Homœopathy, Calcutta, and of the Ashutosh Homœopathic College, Calcutta.

The following categories should be placed on a 'list': (a) Those who are *bona fide* whole-time practitioners of homœopathy for not less than seven years at the time when effect is given to these recommendations; (b) All other categories of existing homœopathic practitioners provided they pass a test both in the theory and practice of homœopathy as may be prescribed by a competent authority. The test should conform to the existing standards as laid down by the General Council and State Faculty of Homœopathic Medicine, West Bengal. The test may be continued for a period of not less than three years and may be held twice a year. Existing homœopathic practitioners who are unable to pass the examination within this period should be debarred from practising homœopathy.

Immediate steps should be taken by the Central and Provincial Governments to declare illegal the use of bogus degrees, diplomas or titles and their colourable imitations.

A distinction should be maintained between a 'register' and a 'list'. Registration is intended to safeguard the public, to facilitate control of practice, to enable practitioners to get rights and privileges of *bona fide* medical practitioners and to protect them against unfair competition by unqualified persons, to provide an electorate for the provincial branches of the Central Board and to protect the public being exploited by quacks.

The registered homœopathic practitioners should be entitled to sign or authenticate a birth or death certificate or a medical or physical fitness certificate and to give evidence at any inquest or in a court of law as an expert. The 'listed' practitioners should not enjoy

any of the above privileges although they will be entitled to practise homœopathy.

Central Council

The Committee has recommended the establishment of a Central Council of Homœopathic Medicine with a whole-time paid Secretary.

The functions of the Council shall be mainly of a co-ordinating and advisory nature, but the Council will have powers to control, which will be exercised through the Provincial Boards or Faculties, in the following matters:—(i) Standard equipment and training of affiliated homœopathic institutions; (ii) Standard of examinations to be held for homœopathic students; (iii) Registration of existing homœopathic practitioners; and (iv) Homœopathic pharmacies, pharmaceutical laboratories and manufacturing concerns. The Council will have full powers of inspection in all matters.

Provincial Boards or Faculties are to be similarly constituted subject to the provision that in all matters coming within the functions of the Central Council, the Provincial Boards will act under the authority of the former with specified functions.

Model Teaching Institution

The Committee recommend that a central model teaching institution be established for the training of under-graduates and post-graduates.

For the preparation and maintenance of 'lists' as proposed above, Homœopathic Councils should be established in Provinces with a Registrar who will be a whole-time paid officer and also act as Secretary to it.

Training in Homœopathy

It is recommended that there should be a single course of training, namely, the university course and the minimum qualification for admission to the course should be the same as laid down by the Indian Universities in respect of the regular system of medicine. The college course should be of the same standard as laid down by the Indian Universities and the duration of the course should be five academic years. The minimum age for admission should not be less than 16 years.

Recommendations regarding research are also made. Facilities should be provided in recognized institutions for research on lines indicated.

It is considered that a person desiring to practise homœopathy as a profession must have what is called actual bedside experience.

There should be an adequate number of homœopathic hospitals and dispensaries under the charge of homœopathic doctors possessing prescribed qualifications. Pharmacies and organizations concerned with the preparation and manufacture of homœopathic drugs in India should be placed on a proper footing and Government should assume the authority to intervene in cases of lowering down of standards, adulteration of drugs, bad dispensing, etc. The education, qualifications and training of dispensers should be laid down.

Government should provide facilities for training in homœopathy in order to give homœopathy a chance to evolve its own genius.

WORLD MEDICAL ASSOCIATION CONFERENCE IN LONDON

INDIAN DOCTORS ATTEND

(Reproduced from Release No. B.F. 2120 issued by the British Information Services, New Delhi)

DELEGATES from 24 countries, including India, attended the General Assembly of the World Medical Association

which has just concluded its three-day session in London. The delegates were welcomed by the retiring President, Professor Eugene Marquis of France. He has been succeeded by Dr. Charles Hill of Britain.

India's two delegates were Dr. S. C. Sen, a member of the New Delhi Medical Association and also a member of the W.M.A. Council, and Dr. R. A. Amesur. Pakistan was represented by Dr. H. Rahman (Secretary of the Eastern Pakistan Medical Association) and Dr. A. K. Sheikh (Secretary of the Western Pakistan Medical Association) who are at present in Britain on study leave.

Apart from India, Pakistan and Britain, the other countries represented at the Conference were Australia, Austria, Belgium, Canada, Columbia, Cuba, Denmark, Eire, Finland, France, Greece, Iceland, Portugal, South Africa, Spain, Sweden, Switzerland, Luxembourg, Norway, Peru and the U.S.A.

Subjects Discussed

The General Assembly had before it for discussion the reports of the five main committees which were at work during the last year. The subjects which the committees have been studying are: social security schemes in different countries; post-graduate education (this is the first attempt that has been made on an international scale to make a survey of the facilities which exist for post-graduate training); the drawing up of an international code of medical ethics; the relationship of the profession to the medical Press; and the examining of the 'standards of medical care and allied subjects'. The committee dealing with the last-named subject is concerned with such subjects as unqualified practice and the advertisement and sale of patent medicines.

The World Medical Association is a voluntary association, formed two years ago, the membership of which is open not to individual doctors but to the national medical associations of the different countries. To a considerable extent the creation of the Association sprang from British initiative. During the war doctors of many nationalities found themselves in London and out of their conversations with the British Medical Association officers and Secretariat came the idea of a world-wide medical federation.

In 1945 the B.M.A. called an informal conference to discuss the project. Later, in 1946, a conference was held in London which was presided over by Sir Hugh Lett, the then President of the B.M.A., and attended by representatives of 33 countries. The first general assembly met in Paris in September 1947, the second in Geneva. The present headquarters are in New York and Dr. Louis H. Bruce of New York is the Secretary-General.

Objects of W.M.A.

The objects of the W.M.A. are:

- (i) to promote closer ties among the national medical organizations and among the doctors of the world by personal contact and all the other means available;
- (ii) to maintain the honour and protect the interests of the medical profession;
- (iii) to study and report on the professional problems which confront the medical profession in the different countries;
- (iv) to organize an exchange of information on matters of interest to the medical profession;
- (v) to establish relations with, and to present the view of, the medical profession to the World Health Organization, UNESCO and other appropriate bodies;
- (vi) to assist all the peoples of the world to attain the highest possible level of health; and
- (vii) to promote world peace.

*Hp.* (9)

DREAMS COME TRUE

An early morning Sunday scene in London on the most important day of their lives—the day sweets came off the ration. The shop will be opening soon, and if they want to be first in the big buy, they had better make up their minds. Junior seems to be the most uncertain—shall it be those there, the ones with toffees inside and chocolate outside . . . or would those last longer. The world seems full of sweets and dreams are about to become reality.



Hp. (10)

DENTAL CLINIC ON WHEELS

A new type of completely self-contained dental clinic on wheels, consisting of a waiting room for six people, a surgery and a combined recovery room and laboratory, and equipped with its own x-ray apparatus and facilities for a technician to make dental appliances has recently been brought into service for the children of Kent, England. At the new clinic the dental officer inspects the teeth of a young boy while the nurse makes an x-ray of a little girl.

Public Health Section

PRIVATE SANATORIA IN CITIES

By T. K. DAYALU

and

S. S. JAYARAM

Bangalore Nursing Home, Bangalore

It is the general medical practitioner that meets cases of tuberculosis in the earliest stages. The efficient working of the anti-tuberculosis campaign therefore depends on the general medical practitioner. Isolation of cases being one of the most important measures in the campaign, especially in a city like Bangalore, all facilities for isolation must be provided. The existing sanatoria are too small to accommodate all the cases, too inconvenient for many and too abhorring for a few. Especially after the advent of streptomycin large numbers of general medical practitioners have started treating cases in the patient's home as nothing better is done in sanatoria save for the cases which require surgical measures. The old tendency of the general medical practitioner was to avoid cases of tuberculosis and send them all to a sanatorium or put them under care of a specialist. So, the rich would for long remain in their houses as they could afford to pay the specialist and the poor would attend as out-patients until their patience was exhausted, they got a seat in the sanatorium or died in their houses, all exposing a good many to the infection. Now it should be expected that large numbers of cases are going to be treated in their houses due to advent of streptomycin and para-aminosalicylic acid. That means that practically every street in Bangalore will have one or more cases of tuberculosis. The liability to infection will increase.

Fourteen per cent of the cases of sputum examination by us in the last ten years collected from cases of all types of lung diseases met with are positive to tubercle bacilli. This does not include the gastric lavage examination for tuberculosis. In more recent times there is a definite evidence of increase* in the incidence of tuberculosis.

So, we suggest the following scheme :—

(1) Starting private sanatoria in each locality by any general medical practitioner who desires to do so much on the same lines as the Lady Willingdon Tuberculosis Clinic, Kempegowda Road, Bangalore City. Each one becomes an isolation centre. The idea is to isolate all diagnosed cases. It must be within the city limits so that relations can fetch them food and attend upon them.

The Government must allot proper buildings and place them at the disposal of the general medical practitioner on reasonable rent. The ward charges should be moderate—say Re. 1 or Rs. 2 per day to the middle classes and Rs. 5 to Rs. 10 per day for special accommodation where one can afford to pay. The patient can arrange for his own diet. Extra charge may be made for medicines and laboratory tests.

To put such an isolation centre in the midst of dwelling houses is bound to meet with loud opposition from the people of the locality and may not find favour with many medical men too. The people in the locality must be educated to know that it is much safer to isolate all cases in one place rather than allow a case in each street where the disposal of sputum cannot be properly attended to.

(2) Intensive course in tuberculosis may be started to teach the general medical practitioner to carry out (a) medical treatment, (b) artificial pneumothorax, (c) pneumoperitoneum and (d) phrenic operations. Cases requiring further surgical measures can be admitted to better equipped sanatoria.

(3) Those who can keep an x-ray apparatus can charge for x-ray work done. And such cases that are unable to meet the x-ray charges can be sent to the nearest Government centre. In this connection, we should like to point out that a simple x-ray plant can be installed for a sum of Rs. 10,000 or less and the Government can help to advance loans on the security of the plant, the debt being discharged in small instalments. If proper work is done, the apparatus will pay for itself.

Each isolation centre shall not have more than 10 beds inclusive of both sexes for a successful working, as it is not possible for a general medical practitioner to look after more cases as a part-time worker.

Initial equipment shall be :—

	Rs.
10 cots	500
10 mattresses	150
20 spittoons	20
10 basins	50
10 lockers	300
3 bed pans	20
3 enema cans	10
Thermometers	5
A. P. apparatus	150
Drugs and other equipment	100

TOTAL Rs. .. 1,305

*We are unable to agree. Tuberculosis is a dying disease.—EDITOR, I.M.G.

Staff :—

- 1 visiting physician.
- 2 trained full-time ayahs to work by shifts.
- 1 boy.
- 1 *thoti* (part-time).

The last three on Rs. 40, Rs. 30 and Rs. 15, respectively each.

Rent, etc.—Rs. 50 per month (controlled rent). Lighting and water charges Rs. 10 per month.

Contingencies.—Rs. 10, including journals Rs. 5.

The monthly expenses will come up to Rs. 200 to Rs. 250. The initial equipment will be well within Rs. 1,500, not including the microscope or x-ray apparatus.

Income.—Even if half the number of beds are engaged taking the average at Rs. 2 per day per bed, the monthly collection will be about Rs. 300. The medicine and treatment charges are extra at the usual rates charged by the individual general medical practitioner.

Cost to the patients.—Ward charges will be Rs. 30 to Rs. 60 per month depending on cost of medicines. The expenses incurred by the patient will not be more than what they would be if he has to go to a hospital or get a medical man to his house. Government must take care to direct cases to the isolation centres in the respective *mohallas* instead of keeping them on the waiting list and reserve the beds in the hospitals for the mofussil cases. The cases which cannot afford any expense and others which require surgical treatment for the duration may be sent to Government hospitals.

The general medical practitioner must inspire enough confidence to this end. There is no doubt that the assistance of a proper specialist is necessary. So, the Government must depute the specialist to visit each centre to help the general medical practitioner. If the patient feels that he can get comfortable accommodation and at the same time facility for good medical aid is given, these isolation centres will be highly attractive, convenient to the patient and attendants, relieve congestion in the existing sanatoria, isolate the sufferers and check the spread of the disease. The sufferer will get earlier aid, and thereby have a better chance of being cured, and the specialist will have an opportunity of doing his job more easily. The general medical practitioner will have every thing to be proud of. Most important, there will be a check on the spread of diseases. The next step is to wait for improvement in the economic condition of the country and discovery of specific remedies to combat the disease.

LATHYRISM IN BIHAR

By S. B. LAI

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LATHYRISM has been reported from the time of Hippocrates. Mention has also been made of this disease in old Hindu literature 'Bhava-prakash' where it is written that the pulse *Lathyrus sativus* causes a man to become lame and crippled and irritates the nerves (Chopra, 1938). In India epidemics of lathyrism have been reported from time to time usually associated with famine and food scarcity. The first outbreak was reported by Colonel Sleeman in 1844. Between 1900 to 1945 outbreaks of the disease in epidemic form have been recorded in Central Provinces, Rewa, Gilgit, the Punjab and United Provinces. In response to an enquiry, it was concluded by Megaw and Gupta (1927) that the disease was mainly confined to a belt which runs across Central Provinces, the east of United Provinces and north of Bihar. Recently Shourie (1945) has reported an outbreak of lathyrism from Central India.

In this paper is given an account of three epidemics of lathyrism which occurred in Bihar and which came to the notice of the author. They were reported from the districts of Patna, Monghyr and Darbhanga. (The first two districts are situated on the south of river Ganges and the third to the north of the river. The districts are all flat country and there are no irrigation facilities, the farmers having to depend entirely on rain for the supply of irrigation water. Darbhanga and Monghyr districts are seats of malaria and the spleen rate is high. In all the districts the entire population is engaged in agriculture. Besides the landlords there are the landless labourers who work in the fields of the former and get wages in kind consisting of the cheapest grains available. *Lathyrus sativus* is known in these places as 'Khesari'. It is a good hardy crop and gives a good yield with the minimum of labour. It is usually planted after paddy is harvested and without any further effort it grows and is reaped after a few months. It is a very favourable crop because it is cheap and easy to grow. It is used for cattle feeding as well.) The green leaves are also consumed after cooking by a large number of people even of the well-to-do classes.

(As a rule there is acute scarcity of vegetables and fruits in the villages except for mangoes during the season. Milk and milk products are either not available to the poor or are available only in negligible quantities. Meat and eggs, because of the high cost, are also very difficult to obtain.)

(The disease started in July 1947 in the villages of Patna and Monghyr districts while in August 1947 in those of Darbhanga district.)

All the persons affected were landless labourers and were very poor economically. They were

engaged as labourers in the fields of the village landlords and were getting wages in the form of grains of the cheapest type. 'Khesari' always formed a major percentage of the wages because it was cheap and easy to grow. (The number of persons affected together with sex incidence is given in table I.

TABLE I
Number of persons affected together with sex incidence

District	Total number of affected persons	Male	Female	PERCENTAGE	
				Male	Female
Patna ..	143	138	5	96.5	3.5
Monghyr ..	27	27	..	100.0	..
Darbhanga ..	49	46	3	93.9	6.1
TOTAL ..	219	211	8	96.2	3.8

It is very difficult to assess the age of the people in villages, and an approximate age incidence of the affected persons is given in table II.

TABLE II

Age groups	Male	Female	PERCENTAGE	
			Male	Female
12 to 16 years ..	15	3	6.84	1.36
18 to 20 years ..	8	5	3.65	2.28
25 and above ..	188	..	85.83	..

Table III gives the intake of calories and different types of food.

TABLE III

Average intake of calories and types of food in oz. per consumption unit/day (affected families)

Name of district	Cereals	Pulses	Leafy vegetables	Non-leafy vegetables	Fats and oils	Flesh foods	Milk and milk products	Fruits and nuts	Condiments	Calories
Patna ..	16.06	13.27	1.15	1.49	0.33	1.06	1.16	0.79	1.18	3,221
Monghyr ..	12.66	10.74	0.56	0.93	0.10	0.44	0.17	0.60	0.71	2,421
Darbhanga ..	25.57	3.29	0.59	1.61	0.07	0.99	0.30	nil	0.13	2,904

TABLE IV

Intake of vitamin and percentage of 'Khesari' in the diet of affected and unaffected families per consumption unit/day

District	Families surveyed	Percentage of 'Khesari'	Vitamin A, I.U.	Vitamin B, mg.	Vitamin C, mg.
Patna ..	Affected ..	74.1	2,834	3.2	24.2
	Unaffected ..	2.0	4,848	1.8	13.6
Monghyr ..	Affected ..	54.2	2,879	1.6	37.8
	Unaffected ..	2.5	4,012	1.9	10.3
Darbhanga ..	Affected ..	79.6	1,830	2.5	42.4
	Unaffected ..	3.5	4,142	1.6	3.0

Types of food consumed

Diet surveys were carried on all the affected families. All the food taken was weighed twice a day, before cooking, for a total period of 10 consecutive days on the lines suggested by Aykroyd and Krishnan (1937). (Altogether the food intake of 150 families consisting of 857 persons was investigated. Diet surveys of the unaffected families were also carried on. For brevity the relevant figures only of the unaffected families are given in table IV.)

Of the cereals consumed, maize, ragi and barley were the most important items, while rice and wheat were in a very small quantity. 'Khesari' was the most important pulse consumed. The consumption of other articles of foods too was below the standard suggested by the Nutrition Advisory Committee (1944). The only source of fats was mustard oil. Ripe mangoes and ripe jackfruits were the fruits consumed by the families in Monghyr while those in Patna were found to take only green mangoes.

Analysis of the diets of the affected and unaffected families for vitamins made with the use of the tables in Health Bulletin No. 23 (1946) is given in table IV.

The affected families of Monghyr were consuming ripe mangoes and ripe jackfruits which have a high carotene content. It is because of this that though the consumption of leafy vegetables, fruits and milk was lower than that of Patna, still the figures for vitamin A are nearly the same.

The intake of vitamin A was below the standard laid down by the Nutrition Advisory

Committee (1944) and the same was true for vitamin C as well.

State of nutrition

In order to assess the state of nutrition, all the children available were examined clinically on the lines described by Mitra (1940) and rated as 'good', 'fair' or 'poor'. Table V gives the results of clinical rating by naked-eye examination.

whether it is a deficiency disease. The low intake of vitamin A by families of Darbhanga district does not reflect the incidence of its deficiency in the children of the place, which may be due to the fact that the children while playing in gardens and orchards consume fruits which could not possibly be recorded in the survey. There does not appear to be significant difference in the incidence of the diseases supposed to be due to deficiency of some nutrients, between the children of affected and unaffected families.

TABLE V

Incidence of state of nutrition amongst children of families affected and unaffected with lathyrism

District	Families surveyed		Rating					
			Good		Fair		Poor	
			Actual	Percentage	Actual	Percentage	Actual	Percentage
PATNA	Affected	{ Boys ..	43	14.4	151	51.0	103	34.6
		{ Girls ..	40	22.3	94	52.1	46	25.5
		TOTAL ..	83	..	245	..	149	..
	Unaffected	{ Boys ..	23	15.8	74	51.3	47	32.6
		{ Girls ..	17	18.2	50	53.7	26	29.8
		TOTAL ..	40	..	124	..	73	..
MONGHYR	Affected	{ Boys ..	40	18.4	98	45.1	79	36.4
		{ Girls ..	30	19.2	76	48.7	50	32.1
		TOTAL ..	70	..	176	..	129	..
	Unaffected	{ Boys ..	30	20.4	90	50.0	60	29.6
		{ Girls ..	20	22.4	70	58.2	40	19.9
		TOTAL ..	50	..	160	..	100	..
DARBHANGA	Affected	{ Boys ..	51	16.1	180	57.1	84	26.6
		{ Girls ..	26	17.6	83	56.4	38	25.8
		TOTAL ..	77	..	263	..	122	..
	Unaffected	{ Boys ..	31	30.4	90	58.4	41	10.9
		{ Girls ..	25	18.2	85	63.1	9	18.6
		TOTAL ..	56	..	175	..	50	..

Deficiency diseases

Aykroyd and Rajagopal (1936) have stressed the value of the presence of deficiency diseases and their correlation with the state of nutrition.

The children of the unaffected families were in a better state of nutrition than those of the affected families. The incidence of phrynoderma and xerophthalmia which are supposed to be associated with the deficiency of vitamin A was not so high as compared with angular stomatitis and caries. There is yet no agreed opinion by different nutrition workers on malocclusion and

× Clinical findings

History of sudden onset of the disease was elicited from a large majority of the patients. They stated that usually on getting up in the morning they felt weakness in legs, which progressed on to their present condition. In a few cases the onset was after an attack of fever. The fever mostly was malaria. The other findings were those of upper motor neuron lesion.

Table VI gives the findings of the survey.



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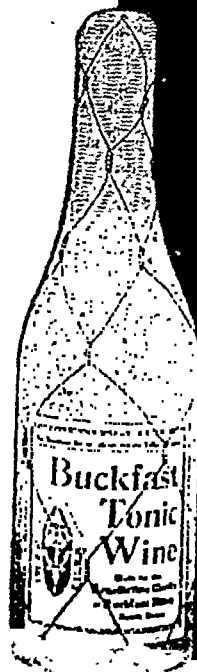
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THE PRINCIPLES & PRACTICE OF TROPICAL MEDICINE

PART II

BY

L. EVERARD NAPIER

C.I.E., F.R.C.P. (LONDON)

FORMERLY DIRECTOR AND PROFESSOR OF
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TROPICAL MEDICINE, SUPERINTENDENT AND
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zoological gardens. The site chosen for the new Central Asylum at Chinsurah (Hooghly) was not considered satisfactory by Colonel Hendley, and another was selected. We cannot help thinking that Chinsurah is far from an ideal site for a central asylum. Hooghly is by no means a popular station, a matter of some importance, as the appointment of the Superintendent of the new asylum is intended to be made attractive and a good man might well hesitate before accepting an appointment, otherwise a good one, when it means residence for many years at a station like Hooghly. The new asylum will be ready none too soon, for the description given of the Patna Asylum by Colonel Hendley and the Superintendent may be summed up in the words of the former: 'Nothing short of demolition is required'.

In the Punjab Asylum's report, Colonel A. Deane, i.m.s., notes a serious and steady rise in the population of the Lahore Asylum. There are only two asylums in the Punjab—at Delhi and at Lahore. The percentage of deaths is considered satisfactory, viz, 9 per cent. Twelve per cent of the daily average strength are reported cured. Pneumonia was more prevalent, possibly due to the intense cold of the winter. A new asylum at Lahore is in course of construction. Surgeon-General Sibthorpe, in the Madras report, notes a steady rise in the epileptic population of the asylums. Many sanitary improvements were introduced, as portable pumps for washing out what are called 'sewage cisterns'. The dry-earth system is in vogue. The Superintendent recommends the artificial heating of certain rooms, a proposal not often heard in India. *Ragi* was the staple grain in use in the Madras Asylum. For destructive maniacs, special garments of canvas and drill, not removable by the wearers, were introduced at the Madras Asylum and proved useful. Gardening, weaving, preparation of grain, mat-making, etc., were the chief occupations of the insanes. Amusements were provided, as in Bengal. The health of the inmates was good; tubercle of lungs caused six deaths out of twenty-six. Surgeon-General Sibthorpe is not satisfied with the nursing arrangements. He suggests that members of the hospital staff should be male and female ward attendants trained in the general hospital for a year, and then transferred to the lunatic asylum for a course of special training in sick-nursing of the insane.

Current Topics, Etc.

Liquid Paraffin Risks

(Abstracted from the *British Medical Journal*, i, 12th June, 1948, p. 1141)

During the late war liquid paraffin (B.P.) for therapeutic use became increasingly scarce, and chemists

were often unable to meet doctors' prescriptions. The scarcity was due partly to diminished production, but increased consumption was undoubtedly the main cause, not for medicinal purposes, however, but because liquid paraffin and indeed other mineral oils were being used as substitutes for fat in cooking. The practice began quite early in the war, and it seemed to increase *pari passu* with the decline in fat supplies. Food and drug authorities tried to check the commercial use of liquid paraffin for this purpose, but they could do little to stop its employment in domestic cookery. Indeed, some voluntary organizations were actively fostering the practice. The Ministries of Food and Health took what steps they could to discourage it, but in the absence of clear evidence showing that harm might result from the regular consumption of liquid paraffin little effective action was possible.

In 1945, at the instigation of the Ministry of Health, workers at the University of Birmingham began to investigate the effects of liquid paraffin, heated and unheated, on nutrition. The biological investigations showed that the daily consumption by rats of raw or heated liquid paraffin (B.P.), in doses up to 2 ml. per 200 g. body weight daily, had no demonstrable effect on the growth or reproduction of rats over two generations. Some interference with vitamin A and carotene absorption was observed, especially when supplements of these substances were added to the diet.

Frazer and his colleagues in Birmingham have shown that liquid paraffin is absorbed when administered in finely dispersed emulsions of particle size less than 0.5 μ . It is not known whether the oil is as finely dispersed in flour products, such as cakes and pastry, baked with liquid paraffin. Whatever the degree of dispersion, however, the continued ingestion over long periods of substantial amounts of paraffin may result in the deposition of paraffin in the intestinal wall, the mesenteric lymph glands, and in the liver. Deposits in these tissues were found at necropsies on persons dying from various diseases who had consumed liquid paraffin for years. Paraffin is not metabolized, and continued ingestion presumably would lead to accumulations of the oil. Though we do not know the precise fate of such deposits, we cannot be indifferent to their presence in the body.

The above objections apply with greater force to the use of ordinary mineral oils as substitutes for fat. This practice has been increasing even more rapidly than that of using liquid paraffin. Most unrefined mineral oils contain small amounts of undesirable substances, even though the absence of colour, odour, and taste might suggest the contrary. In some of these oils cancer-producing substances have been identified.

On the evidence available, therefore, the use even of refined liquid paraffin (B.P.) in the preparation and cooking of food is to be condemned. It has a definite therapeutic value, and its use should be restricted accordingly. In view of the possible risks of continued consumption, liquid paraffin should be taken only on medical advice, and the doctor prescribing it would do well to bear the risks in mind. The internal use of other (unrefined) mineral oils in any shape or form must always be condemned.

Infection through Soaked Dressings

By L. COLEBROOK

and

A. M. HOOD

(Abstracted from the *Lancet*, ii, 30th October, 1948, p. 682)...

The possibility that wound pathogens can readily 'grow through' an intact dressing when this becomes soaked with exudates has been investigated.

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Original Articles

SCHILDER'S DISEASE

By S. K. MUKHERJEE, M.B. (Cal.), M.R.C.P. (Lond.),
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SCHILDER'S DISEASE belongs to the demyelinating group of diseases. It would be interesting to study their incidence. A recent investigation of records of patients in the medical wards of the Medical College Hospitals, Calcutta, showed 1,260 neurological admissions during the period 1937 to 1944. Of these there were only 16 cases of demyelinating diseases of unknown aetiology. These were two cases of neuromyelitis optica while fourteen were disseminated sclerosis. It should be mentioned that demyelination following infectious conditions, e.g. chicken pox, vaccinia, measles, etc., has been excluded.

Ferraro in 1937 published a classification of the demyelinating diseases. According to him, demyelination may be due to infection, toxins or unknown aetiology. Demyelination following measles, etc., is of infective origin. Avitaminosis often brings about demyelination. The known demyelinating diseases are—

1. Acute disseminated encephalomyelitis.
2. Disseminated sclerosis, neuromyelitis optica.
3. Transverse myelitis.

In all these three diseases both the grey and white matters are affected, demyelination develops and is patchy in distribution. Evidences of inflammation are usually present—namely perivascular inflammatory cellular collections in broad areas outside the wall of the blood vessels even up to some distance into the brain matter and the degenerated areas show presence of polymorphonuclear cells, along with the scavenger cells and small mononuclears which are seen in all degenerative conditions of nervous system. Both the nerve cells and the nerve fibres may be affected. Gliosis around blood vessels develops usually.

4. Schilder's disease—a degenerative condition and rarest of all.

Ætiology.—Schilder's disease is known to afflict children, adolescents and young adults;

males are more often attacked, the ratio being 2:1 (Schilder's case was a girl of 14 years). Majority of recorded cases occur sporadically but a familial incidence is now being recognized more frequently. Gasul in 1930 published a brief summary of 71 reported cases. His review included two affected siblings reported by Krabbe (1916) and three reported by Ferraro. Collier to whom we owe much for the clinical identification of this disease postulates that it is due to a primary affection of those neuroglial cells in the white matter which adversely influencing the nutrition of the myelin sheaths cause their degeneration.

White matter of both the cerebral hemispheres undergo degenerative changes. The cord is rarely involved. Only the white matter is affected. The grey matter, both in the cortex and in the nuclei in the base of the brain with its nerve cells, remains perfectly healthy. The cerebellum also remains healthy. Extensive demyelination with subsequent disappearance of the axis cylinder, softening of the nerve fibre, perivascular collaring of cells mainly scavenger cells and early gliosis are the main pathological changes that develop in the white matter in this progressively degenerative disease. The degenerated area becomes very soft, gelatinous, partly translucent with lumps of slightly yellowish glistening oily substance (the separated myelin). When the softening and liquefaction is marked—the degenerated tissue pours out like thick condensed milk.

The degenerative process usually starts at the occipital lobes, but may start anywhere in the white matter of the cerebrum and spreads throughout the white matter. Rarely it may start unilaterally and then spreads to the other side through the corpus callosum which also becomes softened. The collaring of the blood vessel is degenerative in type and not of the inflammatory nature; it is truly perivascular and does not infiltrate into the surrounding brain matter. Gliosis develops around the blood vessels and at the margin of the degenerated area. Onset is usually acute and rapidly progresses to a fatal termination in less than a year.

The main clinical manifestations are early and rapid failure of vision leading to total blindness, impairment of mental faculties and a progressive spastic paralysis. Blindness often begins in one eye and later occurs in the other. Demyelination in the occipital lobe brings about this central blindness. Often optic neuritis with some papilloedema may cause visual failure; and in these cases headache and vomiting are prominent features, suggesting increased intracranial tension. A few may develop blindness through primary optic atrophy. Mental manifestations are characterized in the early stages by dullness, forgetfulness and euphoria. This rapidly progresses to complete mindlessness. Somatic features are those of acute progressive spastic paralysis with all the signs and symptoms

of pyramidal involvement, there may be hæmiplegia or monoplegia. Affection of special senses may occur such as deafness, tinnitus and loss of smell and taste. General sensory changes when present are cortical in origin.

Ataxia may be an early development due to involvement of parietal lobes. Epileptiform fits, generalized or Jacksonian, may appear in any stage of illness. Fever is usually absent but there may be irregular pyrexia and some of the more acute cases have been pyrexial throughout. Cerebro-spinal fluid is usually normal but an increased protein content and slight lymphocytosis are occasionally met with.

Early involvement of both the optic nerves is suggestive of neuromyelitis optica in which spinal paralysis is associated with sensory loss while the cerebral functions remain unimpaired.

In view of the rarity and interesting nature of this disease we thought it worth while to report a case which we have come across recently.

A Case

S. H., aged 16 years, male, was admitted on 1st September, 1948, into the Lake Medical College Hospital under one of us (P. K. Guha) complaining of loss of vision in both eyes of six days' duration. About three weeks previously he suffered from malaise, bodyache and headache associated with fever which was diagnosed as malaria and he was in bed for ten days. He then had an attack of severe headache four days later, following a severe physical exertion and was relieved by analgesics. Two days after this he noticed dimness of his vision and slight deafness. About twenty-four hours later he complained of total blindness with slight ataxia of his lower limbs along with increasing deafness. Patient was of average build and nutrition. His temperature on admission was 97°F. He was dull and slow in answering questions. His hearing was poor and there was complete loss of vision in both eyes. Pupils both central, circular and equal but widely dilated. Both were insensitive to light. Ophthalmoscopy revealed some papilloedema in both eyes. Other cranial nerves were normal. Upper limbs: no abnormality detected. Lower limbs: spastic paralysis with no sensory impairment. Investigations: W.B.C. 4,900 c.mm.—polymorphs 56 per cent, lymphocytes 42 per cent, monocytes 1 per cent, eosinophils 1 per cent. Blood for Wassermann reaction and Kahn negative. Lumbar puncture revealed cerebro-spinal fluid of normal pressure and colour, having 3 lymphocytes per c.mm., 55 mg. of sugar per 100 cc. and 690 mg. of chloride per 100 cc. On culture C.S.F. was sterile.

Gradually he became more restless and delirious, later passed into coma with retention of urine, and developed a temperature of

102°F. with signs of bronchopneumonia which terminated fatally on 19th September, 1948.

Autopsy findings.—Body of average build. Rigor mortis present in legs. All the viscera were found congested. No other significant abnormalities were detected in any organ excepting the brain and cord which are described in detail.

Brain—Dura and leptomeninges were congested. No abnormality detected on the surface of brain. The whole brain was very soft. After removal on being kept on the table the brain lost its normal shape and flattened out. During the examination the corpus callosum began to tear off. The frontal lobe was punctured with a knife and a lump of soft creamy substance with glistening oily material at places came out. On horizontal section the whole of the white matter of brain in both the hemispheres, with the exception of a very small area at the extreme posterior end of the left occipital lobe, was found to have undergone extreme softening and looked like the matter that came out of the brain through the puncture made. The remaining portion of the corpus callosum was torn on slightest handling. The nuclei thalamus caudate nucleus, etc., were found intact with no evidence of degenerative changes. Within the remaining healthy white matter at the posterior end of the left occipital lobe, there was a small round softened area less than a quarter inch in diameter.

Cerebellum did not show any abnormality. There was not a single hæmorrhagic area in the whole brain and cord (figure 1, plate XXVIII).

Spinal cord was next examined. Greyish areas with injected blood vessels over them were found at the levels of 7th cervical and 10th thoracic specially at the level of 10th thoracic. The first area was more or less soft but the area at the 10th thoracic appeared slightly flat and felt very soft. On section at this level softened whitish material bulged out and the differentiation between white and grey matter was completely lost. In the other soft area the differentiation was not very clear. The lumbar and cervical enlargements and the cauda equina did not show any abnormality. Other areas on section were normal in appearance.

Examination of the creamy material: Smears stained with Gram stain and with Giemsa's stain showed a large number of scavenger cells (phagocytic cells originating from microglia cells), a few rod cells (elongated cells in the process of transformation from microglia to scavenger cells), a few small round mononuclear cells with compact nucleus, occasional astrocyte-like cells with processes, and granular debris. No acid-fast bacilli nor any other bacteria or parasites were found by microscopical and cultural methods. No special investigations for virus were made.

Morbid anatomy.—(a) In the cortical portion (grey matter) of brain no evidence of degeneration or of inflammation was found. The nerve cells were found healthy with intact axis cylinders attached to them. Most of the cells showed Nissel's granules. The pattern of the matrix was normal. The membranes at the surface showed congested capillaries (figure 2, plate XXVIII).

(b) The degenerated area began a few millimetres under the grey matter. At the margin of the degenerated area typical collaring of blood vessels by mononuclear cells was noted. No infiltration of cells could be seen in the brain matter proper. The degenerated area showed a loose matrix composed of great concentration of scavenger cells, a few small mononuclear cells and rod cells and debris. The wall of the blood vessels even in the degenerated areas were found healthy and within the degenerated zone itself collaring of blood vessels could be noted, but the collection of cells here was not very marked everywhere. A piece from the circular degenerated area on the left occipital lobe showed similar picture limited on one side by healthy grey matter and on the other side by more or less degenerated white matter with thinly scattered round cells. Gliosis along the border of the degenerated area was not seen but slight increase of glial fibres were seen around blood vessels (figure 3, plate XXVIII).

Spinal cord—Showed similar picture; the nerve cells in the horns were found healthy.

Comments

This was a very acutely developing case and proved fatal very quickly within a period of 6 weeks. Practically the whole of the white matter of both the hemispheres and the corpus callosum were degenerated in 25 days as far as it can be judged from the date of manifestation of symptoms. Due to this rapid degeneration the symptoms developed so quickly and the development of gliosis, etc., was very poor. No evidence of infective inflammatory changes seen. Nor any other causative factor which might cause such extensive degeneration could be detected.

The spinal cord symptoms developed also very quickly due to early involvement of cord and the signs of upper motor neurone lesion were masked.

The clinical differentiation from neuromyelitis optica became difficult because of papilloedema and spastic paralysis. But later the conspicuous absence of spinal sensory signs together with profound impairment of cerebral function made it possible to make a clinical diagnosis.

This case was demonstrated at a clinical meeting of the Ophthalmological Society of Bengal in September 1948, when some ophthalmologists and general physicians thought that the patient was suffering from neuromyelitis optica. Dr. S. C. Chatterjee, M.B., M.R.C.S. (Eng.), M.R.C.P. (Lond.), however, was in full

agreement with us regarding our provisional diagnosis of Schilder's disease and we are grateful to him for his valuable assistance in the diagnosis of this case.

We thank the Superintendent, Lake Medical College Hospital, for his permission to report this case and thank also Dr. D. P. Lahiri, Senior Clinical Pathologist, who conducted the post-mortem examination. We are grateful to Dr. B. P. Tribedi, Professor of Pathology, Calcutta Medical College, for allowing us the photomicrographs.

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THREE CASES OF ENCEPHALITIS LETHARGICA

By V. M. BHAT, B.A., M.B., B.S.
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DR. KUNDU's article in the July 1949 issue of the *Indian Medical Gazette* prompts me to publish three cases of *Encephalitis lethargica* which occurred in one family at Yeola, an out-of-the-way town in Nasik District, Bombay Presidency.

First two cases deceptive

On 28th May, 1949, the son and daughter of one of our colleagues were, all of a sudden, attacked with what appeared, at first sight, to be symptoms of cholera or food poisoning. Both were aged 9 and 7, respectively. (Cholera was somewhat prevalent in the adjoining villages.) Both had one or two watery motions each and both vomited twice. They had nausea also and were complaining of giddiness. This had occurred in the afternoon. Yet the children were moving about till the evening. Their mother got alarmed at their increasing giddiness and nausea, and sent for their father. He, being a doctor, found them somewhat uneasy, and thought that they were possibly suffering from a mild attack of cholera or food poisoning, and administered some gastric sedatives.

Coma and pulmonary oedema

In the evening at about 6-30 p.m. the boy suddenly became comatose. His temperature

was 101°F. But the pulse and respiration rates were much disturbed—16 respirations with a pulse rate of 120 per minute. The girl became drowsy and completely comatose at 8 p.m. and was becoming worse and worse every hour. I was called in at about 9 p.m. The girl was acutely ill. Her temperature was 102°F. The respirations were slow. Her chest was full of râles and she showed all the symptoms of pulmonary œdema, and was getting cyanosed. The heart was flickering. She was at once given atropine 1/50 gr. by injection and coramine also by the same route. Yet there was no improvement. Lobeline was also administered along with coramine subcutaneously. As the respiration was failing, artificial respiration was resorted to. At about 10 p.m. blood-coloured foam was coming out of the mouth on compressing the chest and the child was gasping. We had almost given her up as dead, although artificial respiration was being continued. Again atropine 1/20 gr. with coramine 1 cc. was given. For a minute or two, respirations were stopped altogether, it seemed. But on compressing the chest, the child heaved a sigh, and our hopes were again revived. We continued the same treatment till about 2 a.m., when respirations and heart resumed their rhythm, and were somewhat steadied. The temperature rose to 104°F. at that time.

Her brother's condition was not so bad. But as the rate of respiration was slower than normal, we administered atropine 1/50 gr. and 1 cc. coramine to him also, once or twice, during the night. Glucose water with a little brandy was given to both the children in sips. The patient's father with Dr. P. S. Mahajan and myself were struggling for the whole night, and had the satisfaction that the girl was almost rescued from the jaws of death. The next morning, the boy became conscious, and was prancing about in the afternoon. The girl continued to be comatose, but her heart and respirations had resumed their rhythm. The temperature was 103°F. in the morning, and she was able to take sips of glucose water. As the temperature was high, cold compresses were put on the abdomen and forehead.

No diagnosis: Treatment symptomatic

Although we were treating both the children symptomatically, still none of us was sure about the diagnosis. Cholera or food poisoning theories did not fit in the picture. But as the boy had apparently recovered—I say apparently because his case had become chronic, and he was to cause constant worry and anxiety to all concerned for 3 months—our minds were somewhat at ease, and we hoped that the girl too would recover soon like her brother.

Masking meningeal symptoms

Next morning the girl began to show symptoms of meningitis. Her neck was stiff, eyes were

congested, and Kernig's sign was present. The temperature was 104°F., and the coma continued. At once we decided upon penicillin, and gave her 3 lakhs units during the 24 hours. Glucose was administered intravenously twice a day, in addition to glucose water and milk by mouth. But many a time she could not swallow anything by mouth, and the liquids trickled down the cheeks. Glucose-saline enemata were also sometimes rejected. Urine had sometimes to be drawn by catheter. Bowels were emptied by glycerine syringe or enema. Cylotropin was sometimes given on the theory of meningeal infection. The girl continued in this comatose condition for full 9 days in spite of the treatment, with cibazol, coramine and sometimes digitalis by mouth or parenterally in addition. On the 10th day she showed some signs of returning consciousness. She began to cry and wince if pricked, and opened her eyes and cried for her mother. She began to take her feeds regularly. Penicillin was continued in smaller doses till the temperature dropped down to normal. Protein hydrolysate was given for protein deficiency, and she made a rapid recovery in about 4 weeks.

Just before the girl was rallying round, the idea struck me that these may be cases of *Encephalitis lethargica*, and I expressed my opinion to the father of the patients. But as the girl's case was masked by meningeal symptoms, I could not arrive at definite diagnosis. The cases were occasionally discussed in consultation with my colleagues here, but none could express a positive opinion about encephalitis, as there were no clear-cut signs and symptoms of that disease.

Third case clears up diagnosis.

Unfortunately, on 6th June, 1949, possibly by prolonged mental strain and vigil for so many days and nights, the mother of the children began to show symptoms of illness. She developed diplopia, ptosis, insomnia, giddiness, garrulity and symptoms of mental aberration. An affectionate mother as she was, she began to show complete apathy towards her ailing daughter, who wanted to cling to her. She railed against her near and dear relatives and her lady friends. She refused food and drink. She developed something like paranoia. She was however conscious and could recognize others. Her temperature was slightly above normal.

The mother's symptoms clinched the diagnosis which was agitating my mind for about two to three weeks. I pored over all the available authorities, Osler, Price, Savill and various medical annuals from 1925 to 1937, and came to the definite conclusion that all the three were cases of *Encephalitis lethargica*. Her symptoms definitely pointed to that. Hysteria suggested itself, but was ruled out, as she had never shown any of its symptoms before.

Besides, three cases, occurring in the same family, one after another, with initial drowsiness, coma, and definite symptoms in the third case, and absence of any history of hysteria before, pointed to encephalitis and not to hysteria. Subsequent histories of the three cases left no room for any doubt.

Relapses and laboratory investigations

The mother was treated on the same lines as the girl. In addition, she was given nervous sedatives. But as she was in a suicidal mood for some days, she point blank refused to take any treatment or nourishment. She had to be coaxed to take homeopathic treatment, and we succeeded in smuggling some barbitones into it. And we had to be content with it, as there is no specific treatment for encephalitis. She recovered for a time, but again relapsed into a second attack and after a few days into a third attack, with all the symptoms of diplopia, drowsiness, ptosis, giddiness and even some traits of Parkinsonism. She took nearly six weeks for recovery.

After a month or so after her recovery, the girl also had one relapse on 17th August, 1949. But it was very mild in character. She had blurred vision, ptosis, drowsy look and giddiness. She, however, recovered within 16 hours.

Chronic cases

Unfortunately the boy, on whose sudden recovery we congratulated ourselves in the first instance, had a very severe relapse on 2nd August, 1949. He became drowsy, had diplopia, blurred vision, ptosis, giddiness and Parkinsonism. But when not drowsy, he was very violent, kicking and biting his mother and others, sometimes he was so uncontrollable that his hands and legs had to be tied down. Even in this condition, he was rolling himself to catch his mother and have a bite of any of her part he could reach. This relapse lasted for 3 days, and he recovered from it completely on the 4th day.

These relapses left no room for any doubt about the diagnosis.

As our resources of treatment were exhausted, and to confirm the diagnosis by the examination of C.S.F., we decided on the 18th August, 1949, to send the patients first to Ahmednagar where all the facilities were available under the able direction of Dr. Anderson of the Evangelical Booth Hospital. He took the C.S.F. of every patient by lumbar puncture and made a thorough examination of all the patients.

Blood of all was negative for malarial parasites. Yet one doctor thought that the boy might be suffering from cerebral type of malaria. The boy's case was causing us more anxiety. He confirmed my diagnosis and advised his father to try procain penicillin 1 cc. containing 3 lakhs units for 10 days and some sedatives.

C.S.F. examination

	Boy, 19-8-49	Girl, 19-8-49	Mother, 20-8-49
Appearance ..	Clear	Clear	Clear
Albumin ..	nil	nil	nil
Sugar ..	nil	nil	nil
Globulin ..	Negative	Negative	Trace
* Cell count ..	84 per c.mm.	5 per c.mm.	3 per c.mm.
T.B. ..	Negative	Negative	Negative

* On 1st September, 1949, again the C.S.F. was examined and the cell count was 1 or 2 per c.mm.

When they all arrived here, the boy got a second violent relapse on 2nd September, 1949, with all the symptoms described above. Parkinsonism was more evident now. But one peculiar feature in these two relapses was that his neck muscles became as if partially paralysed. Due to this and Parkinsonism, he used to fall on his face, and sustain minor injuries.

Then on 9th September, 1949, he was taken to Bombay where he was thoroughly examined over again by Drs. Coelho, Tulpule and Wad. They confirmed the diagnosis but could not suggest any specific treatment against the virus. They expressed the fear that the boy might develop epilepsy and suggested prominal and other sedatives with siolan-iodine 2 cc. twice a week for 4 times only.

Then this chronic patient started getting the attacks every 10th day or sometimes even sooner than that. According to Price, the course is variable, and Savill says that 1/3 of the cases die, and 1/3 seriously disabled. I conjectured that this patient would fall in this category of disablement. The boy was taken to Poona also with a view to showing him to Dr. Bhagvat of the mental asylum. He also suggested sedatives like luminal or prominal to be given in small doses daily. His blood sugar was 83.3 mg. per cent.

The mother of the two children affected had to go to Ujjain as her father had an attack of paresis, about a month previously. She took both her children with her, as they were free from relapses. She and her children returned here on the 3rd November, 1949. On Saturday the 5th instant, both the children had severe relapses or fresh attacks, I can't say which. These attacks of encephalitis resembled the original attacks and were so severe that the girl expired in comatose condition after 20 hours due to respiratory failure primarily. Her lungs were so much cedematous that venous blood was trickling down her nose and mouth. She had been given atropine, lobeline, coramine, adrenaline by injections along with glucose saline, but to no purpose.

The boy was also affected on the 5th instant at night. He had slept well for an hour or so, but as was subsequently known, then become unconscious, and could not be roused. His

stertor drew our attention to him. He was given the same treatment as was given to his sister. His pulse was good. Next morning he woke up, and was quite conscious till 2 p.m. He took his food also with his own hands. But at 2 p.m. while asleep, his respiration began to fail, and he became comatose. Again the same gamut of treatment was gone through, and penicillin was started as his temperature was raised. Two lakhs units were given initially, and the same dose was repeated at night. His lungs too became oedematous, and venous blood came out every time when artificial respiration was resorted to. Gradually the number of respirations began to increase from 8 to 16, and then to 34 at night, with a pulse rate of 140 to 160, and temperature hovering between 102 to 105. Cerebral congestion was fully evident as his eyes were red on the next day. Artificial respiration had to be resorted to every time when the number of respirations fell below 12. Tuesday and Wednesday (i.e. the 8th and the 9th November) passed in the same condition without any improvement. Nothing could be given by the mouth, and dehydration was combated with glucose saline intravenously and subcutaneously. On Thursday morning some pus trickled down the nares, and blood had to be cleared out of his throat every few minutes. Eyes were very red, and both the corneas resembled ground glass. On the 10th instant respiratory failure again supervened, and the boy died at 6-30 p.m. in the evening.

Fortunately the mother, who had a mild attack, has survived in spite of these shocks.

Points for consideration are: (1) whether these attacks after nearly a few months were fresh ones or mere severe relapses. There is some ground for suspicion on this point; because the children were infected at their grandfather's house at Indore in the first instance, when they had been there in last May. Later also they had been to their grandfather, but this time he was at Ujjain. Possibly his attack of paresis may be one to the infection, and he was the carrier. (2) I have never come across an instance of death in relapses as no authority mentions it anywhere in the literature. And it came a few months after!

[This account was received in two instalments which have been combined. The second instalment gave the fatal ending. The diagnosis of polio also needs a consideration.—Editor, I.M.G.]

A STUDY OF THE BACTERIOLOGICAL TYPES OF *C. DIPHTHERIAE* IN BOMBAY

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and

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SINCE Anderson *et al.* (1931) first introduced tellurite medium in the diagnosis of diphtheria,

the recognition of the three types has become almost a routine procedure in all public health laboratories in foreign countries, on account of their epidemiological significance. Not much attention has been paid to this aspect in India, as no work on these lines has been reported anywhere in this country. Laboratory workers in India seem to be satisfied with the use of Loeffler's medium in the diagnosis of clinical diphtheria. The statement of Cooper *et al.* (1940) that bacteriologists who continue to depend entirely on Loeffler's medium are doing second-rate bacteriological work so far as diphtheria is concerned, was a serious reflection on any well-established laboratory. Since the statement appeared, we have tried our level best to incorporate tellurite media in the routine diagnosis of diphtheria at this Institute, but the irregular and inadequate supplies of potassium tellurite during war prevented us from doing so. With an adequate supply in 1945, an opportunity was provided, which enabled us to make a comparative study of Loeffler's and tellurite media in the primary isolation of *C. diphtheria* and incidentally to study the type met with in Bombay. The investigation was carried out for a period of nearly 9 months and 175 strains of *C. diphtheria* were isolated and studied, with reference to the bacteriological types. Further a comparative study of Loeffler's medium and tellurite medium for primary isolation of strains in 127 cases was made.

Material for present investigation was chiefly received from the City Fever Hospital for Infectious Diseases. Private practitioners also contributed to a small extent, the diagnostic service for any infectious diseases being free at this Institute. Throat swabs of patients admitted into the hospital were first cultured on Loeffler's medium and examined microscopically by the hospital staff. The Loeffler's slope and the swabs were then sent to this Institute for further report. On receipt of the swabs, they were teased in 0.5 cc. of broth and a 2 mm. loopful of the resulting suspension was spread on a Loeffler's slope and also on Neill's tellurite medium. Loeffler's original medium was modified as suggested by Goldsworthy and Wilson (1942) by passing the serum-glucose mixture through a Seitz filter and inspissating the same in tubes at 85°C. for 2 hours. Neill's (1937) tellurite medium was adopted for plating as it was found to be simple and convenient. Loeffler's slopes and tellurite plates were examined after 24 hours and 48 hours' incubation respectively for presence of *C. diphtheria*. Pure cultures from single colonies were obtained from both the media and they were studied further as regards the morphology, colony appearance, biochemical reaction and virulence. Morphology was studied in stained smears using Gram's stain and Albert stain, the latter being excellent for demonstration of metachromatic granules. Colony appearance was studied from the tellurite plate

using hand lens or low-power microscope whenever necessary. The usual substrates for fermentation tests were serum-peptone-water tubes containing (1) 1 per cent glucose, (2) 1 per cent saccharose, (3) 0.5 per cent starch and (4) 0.5 per cent glycogen and they were observed after 48 hours and then kept for 7 days for final examination. In addition a tube of nutrient broth was inoculated to study the character of growth at the end of 24 hours. Hæmolytic activity of the strain was tested on blood agar slopes at the end of 48 hours. Virulence tests, whenever indicated, were done on guinea-pigs, using intradermal technique, including always a fully virulent and avirulent strain as a control.

Results

The total number of throat swabs examined during a period of 9 months was about 500. One hundred and seventy-five strains of *C. diphtheriæ* were isolated and typed by the methods described above. Nine strains were isolated from nasal diphtheria, 1 strain from a cutaneous lesion and the rest 165 were derived from cases of clinical diphtheria.

A comparative study of Loeffler's medium and Neill's tellurite medium for primary isolation of *C. diphtheriæ* illustrates the following results in 127 cases.

TABLE I

Showing the number of strains isolated on two media

Loeffler's medium	Neill's medium	Number of strains	Percentage isolated
+	+	119	93.7
+	-	3	2.3
-	+	5	4.0

One hundred and seventy-five strains, classified according to their types, are shown below :

Gravis type	7
Intermediate type	1
Mitis type	167
			175

Discussion

Direct smear examination.—A brief account of the difficulties met with in the diagnosis of diphtheria may not be out of place here. The value of direct smear examination from throat swabs has been questioned in recent literature. Most bacteriologists are agreed to abandon it from routine. But the practice of reporting on throat swabs is still retained here with a view to giving rapid diagnosis. On some occasions, it has been our experience that a preliminary negative report on a direct smear has to be

followed by a positive report on culture. The value of direct film is not confined to its ability occasionally to reveal *C. diphtheriæ* only; an early report of the presence of large number of streptococci or organisms of Vincent's angina is often helpful to the clinician. However, with the predominance of mitis strains in Bombay and with typical morphology, chances of mistaken diagnosis are greatly reduced. In a small number of comparative observations on diagnosis by direct smear and culture 75 to 80 per cent of smear examinations have been reported correctly by us.

For over 50 years Loeffler's medium has been universally used in the bacteriological confirmation of a diagnosis of diphtheria. Many media have been suggested for isolation of *C. diphtheriæ* but they are either modifications of the standard Loeffler's medium or tellurite medium first described by Anderson *et al.* (1931). Since the advent of tellurite media, many workers are increasingly dissatisfied with the use of Loeffler's medium. Amies (1945) and others tried to modify it, Forbes and Lane (1945) report better results with coagulated plain serum instead of the serum-glucose mixture. Yet another modification by Goldsworthy and Wilson (*loc. cit.*) is to replace inspissation of the mixture by 2 hours at 85°C. after preliminary Seitz filtration. This modification has really been simple, time-saving and suitable, and therefore it has been adopted for routine use in this Institute. The chief advantage of the Loeffler's medium is the speed of growth of many diphtheria strains, which can be detected in six or more hours before colonies on tellurite media make their appearance; at the same time its weakness to allow diphtheroids to grow and its failure to distinguish the gravis and intermediate types on account of their non-granular and short forms resembling Hoffman's bacilli, is well known. The medium is again helpless against a chance sporebearer, which reduces the surface rapidly to a fluid condition, choking the few diphtheria bacilli that may be existing. In this series, although we had not enough opportunities to be familiar with gravis and intermediate strains, we failed to isolate the organisms on some occasions either due to overgrowth of diphtheroids or to the presence of sporebearing bacilli.

Cooper *et al.* (*loc. cit.*) have made a comparative study of half a dozen tellurite media and Loeffler's standard medium for primary isolation of *C. diphtheriæ*. They favoured the use of Neill's medium in conjunction with Loeffler's to secure the maximum positive results. Neill's medium was selected by us as it was simple to prepare and the morphology of the organisms growing on it was not affected to the same extent as it does with the McLeod's medium. Numerous workers have shown that in cases of diphtheria, the causative bacillus can be demonstrated by

tellurite medium in about 5 to 10 per cent more swabs than by Loeffler's medium (Cooper *et al.*, *loc. cit.*) because the latter misses some of the most serious types of diphtheria, *e.g.* gravis and intermediate. In our series, in table I, only 4 per cent strains could have been missed, in the absence of tellurite medium.

We have formed a more favourable opinion of Loeffler's medium than other workers because most of our strains were of the mitis type. The results in our series are also quite in agreement with those reported by Shone and his colleagues (1939), who in a survey of 1,501 cases found 92.4 per cent positive on both media, 2.3 per cent by Loeffler's and 5.3 per cent by tellurite only. As no one single medium is ideal or perfect, the combined use of a Loeffler's slope and a tellurite-blood-agar culture allows a high proportion of all cases of diphtheria to be diagnosed bacteriologically within 18 to 24 hours. It has now been the routine of this laboratory to use Loeffler's medium in combination with Neill's tellurite plate for every swab from a diphtheria case.

Study of strains isolated.—One hundred and seventy-five strains of *C. diphtheriae* were isolated in pure culture from Loeffler's slope or tellurite plate and the colony appearance of each strain was studied on Neill's tellurite plate. Out of 167 mitis strains, 165 showed the usual pattern on the tellurite plate. But with two strains the colony appearance resembled that of the gravis type but the organisms failed to ferment starch and glycogen even in 7 days. Out of 7 gravis strains, 2 showed colonies like mitis but fermented starch. Such atypical strains probably form a very small percentage. According to McLeod (1943), Carter in Glasgow found them to the extent of 0.25 per cent in 1,600 strains but Wright in South Africa, in a small series, observed 13 per cent of such strains. In his opinion atypical strains are only significant if they appear with sufficient frequency and are found to be definitely associated with serious clinical diphtheria. All our four atypical strains were isolated from clinical diphtheria cases moderately severe. Majority of our gravis strains while fermenting starch, failed to ferment glycogen. Besides half the number produced uniform turbidity in broth without much pellicle formation. In two mitis strains, growth in broth was found to be granular, with a deposit at the bottom and the supernatant fluid clear. Haemolysin production as tested on blood agar slopes was found to be a variable feature of the mitis types. All our gravis and intermediate strains showed no haemolytic colonies.

Virulence test.—A study of large number of gravis and intermediate types by various workers has shown that these strains when isolated from clinical cases of diphtheria are invariably virulent as tested on guinea-pigs by subcutaneous or intradermal route. In this series only 40 strains were tested by the intradermal route on guinea-

pigs using a known virulent and avirulent strain as control. Out of 37 mitis strains tested, 33 were found to be virulent. Out of 7 gravis strains isolated, only 2 were tested and they were found to be virulent. One intermediate strain isolated from a faucial diphtheria case gave a doubtful reaction when tested first and proved to be avirulent by repeated tests. One of the mitis strains isolated from a cutaneous abscess on buttocks was found to be avirulent. The very small number of gravis and intermediate strains in our series precludes us from any general conclusions regarding this aspect.

TABLE II

Showing the results of virulence test on 40 strains

Type	Number tested	Virulent	Avirulent
Gravis ..	2	2	0
Intermediate ..	1	0	1
Mitis ..	37	33	4
TOTAL ..	40	35	5

Conclusions

From the observations made by us, we are of the opinion that direct microscopic examination of the throat swab should not be altogether dispensed with; besides, being helpful in rapid diagnosis of diphtheria, it may reveal the presence of other pathogenic organisms such as spirochaetes and fusiform bacilli or streptococci. It has been shown that no one single medium or a combination of two media can be perfect in the isolation of this organism and when it is observed from the results in our work that the preponderant bacteriological type is mitis in Bombay, Loeffler's medium cannot be set aside entirely and replaced by a single tellurite medium. The combination of these two media however has given the maximum positive isolations and has therefore been adopted for routine use in this laboratory.

Summary

1. Out of 174 strains of *C. diphtheriae* isolated from clinical cases of diphtheria in Bombay, 167 strains were identified as mitis, 7 as gravis and 1 strain as intermediate.

2. Since the predominant type of *C. diphtheriae* was 'mitis', virulence test was carried on some of these strains. The test showed that 89 per cent of them were virulent. A mitis strain isolated from a cutaneous lesion and an 'intermediate' strain isolated from a faucial diphtheria case were found to be avirulent.

3. A comparative study of Loeffler's medium and Neill's medium for primary isolation of *C. diphtheriae* showed that 92 per cent of strains could be isolated from both media, 2.3 per cent on Loeffler's medium only and 4 per cent on Neill's medium alone. A combination of these two media was therefore recommended for routine use.

The authors wish to thank the Superintendent of the City Fever Hospital for Infectious Diseases, Bombay, for supplying them with the clinical material for examination and investigation.

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INFECTIVE HEPATITIS*

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Object.—This investigation on infective hepatitis was carried out with the object of finding out the biochemical changes occurring in blood, faeces, urine, etc., and to obtain any data which may be of significant value.

In the following account the disease has been divided into three stages, the acute or pre-icteric, the progressive or icteric, and the recovery or post-icteric stages. Such division is purely arbitrary, as each stage merges imperceptibly into the next; and in certain cases the chief characteristic symptom, jaundice, was absent altogether. Nevertheless the classification is instructive, particularly in considering the various biochemical changes that occur throughout the course of the disease.

* This work was carried out in 1943 while the writer was attached to the Central Military Pathological Laboratory of India, Poona. An epidemic of infective hepatitis broke out in Burma General Hospital, Hoshiarpur (Punjab). The writer was detailed by General Headquarters to investigate this epidemic and the equipment, etc., for the investigation was provided for the C.M.P. Laboratory.

PART I—BIOCHEMICAL

Urine.—An accidental but significant finding was that of amino-acid crystals present in the concentrated urine, which was previously treated with lead acetate to precipitate proteins, and absolute alcohol to eliminate urea. Amino-acid crystals were present in 22 cases (36 per cent), as detailed below :—

Leucine, tyrosine and cystine	..	1
Leucine and tyrosine	..	4
Leucine only	..	13
Tyrosine only	..	2
Cystine only	..	2

Out of the 22 cases showing amino-acid crystals, 18 showed leucine either in pure, transitional or impure forms. In a certain percentage of cases these crystals were persistently present for over a month.

The percentage of these crystals in urine bore no relation either to the intensity of jaundice or the gravity of clinical symptoms but cases in which they occurred ran a more protracted course and convalescence was delayed.

It has been observed that bile salts disappear last from urine, taking as much as a fortnight to 2 months after jaundice had disappeared. Urobilinogen appears to be the earliest to be increased; while the excretion of bilirubin in urine was associated with pale or clay coloured stool.

Stools.—In the early stages of the disease the stool has normal colour and consistency, but later becomes pale or clay coloured, and in some cases bulky and frothy, depending on the amount of unabsorbed fats. The change in colour is partly due to deficient bile and partly to the fatty nature of the stool. Complete absence of bile is noticed in a very small percentage of cases and the duration of such complete absence is short, being on the average 7 to 10 days. It should be added that pale or clay coloured stool does not indicate absolute absence, but only a diminished excretion of bile.

Faecal fat analysis was carried out in 22 cases, and the chief characteristic feature found on fat analysis was universal increase in the free fatty acids, irrespective of whether the total fat content was normal or increased in quantity, indicating a dysfunction of fat absorption rather than fat digestion. These findings were noticeable both on low and normal fat diet.

Liver efficiency tests

The liver efficiency tests are divided under two groups :—

- Tests depending on excretion of bile.
- Tests not depending on excretion of bile.

A. Tests depending on excretion of bile

I. Van den Bergh reaction (normal 0.2 to 1.0 van den Bergh units)

Quantitative van den Bergh reaction was carried out in most cases at various stages of the disease. At first a biphasic delayed or biphasic prompt reaction, later changing to biphasic prompt or direct immediate reaction, was observed; thus indicating toxic or infective nature of the lesion, giving rise later to reaction pointing to obstruction. The results of the quantitative van den Bergh may be summarized as follows :—

Stages	Van den Bergh units	Number of cases	Percentage
Acute ..	0.2- 1.0	<i>Nil</i>	<i>Nil</i>
	1.0-10.0	9	56.2
	10.0-20.0	6	37.5
	20.0 and over	1	6.3
Progressive	0.2- 1.0	<i>Nil</i>	<i>Nil</i>
	1.0-10.0	20	90.1
	10.0-20.0	2	9.9
	20.0 and over	<i>Nil</i>	<i>Nil</i>
Recovery ..	0.2- 1.0	13	65.0
	1.0-10.0	7	35.0
	10.0-20.0	<i>Nil</i>	<i>Nil</i>

As jaundice increases in intensity, serum bilirubin also increases. Icterus index which was carried out concurrently corresponded to the results of van den Bergh reaction.

II. Phosphatase activity (normal 0.1 to 0.21 Kay's units)

Serum phosphatase activity was estimated at various stages of the disease. The results may be summarized as follows :—

Stages	Kay's units	Number of cases	Percentage
Acute ..	0.1 -0.21	<i>Nil</i>	<i>Nil</i>
	0.21-0.50	1	6.8
	0.51-0.90	7	46.6
	0.91-1.30	7	46.6
	1.31 and over	<i>Nil</i>	<i>Nil</i>
Progressive	0.1 -0.21	<i>Nil</i>	<i>Nil</i>
	0.21-0.50	17	48.2
	0.51-0.90	11	31.4
	0.91-1.30	4	11.4
	1.31 and over	3	8.6
Recovery ..	0.1 -0.21	16	48.5
	0.21-0.50	12	39.4
	0.51-0.90	4	12.1
	0.91-1.30	1	3.0
	1.31 and over	<i>Nil</i>	<i>Nil</i>

Correlation between serum bilirubin and phosphatase.—In liver disease, the excretion of bile can be prevented either by blockage to biliary canaliculi or by necrosis of liver cells, or

by both; and bile is reabsorbed either by way of lymphatics or directly back into blood, thereby increasing the bilirubin content of blood. In cases of infective hepatitis, bilirubin content and phosphatase activity begin to increase, but such increases bear no relation to each other. And if the increase in either is due to biliary obstruction, it is probable that the nature of obstruction is different in two cases. The lack of relationship displayed is probably due to the fact that bilirubin is raised when bile passages are obstructed whereas phosphatase activity is elevated as a result of intrahepatic obstruction caused by necrosis of liver cells, and presumably is proportional to such necrosis (Weil and Russell, 1942).

If serum bilirubin increase is due to obstruction to biliary canaliculi, whereas phosphatase activity increases as a result of obstruction to bile flow caused by necrosis of liver cells, it may be added that presumably in infective hepatitis cellular necrosis is predominantly present and is giving rise to blockage of biliary canaliculi decreases and consequently van den Bergh comes to lie in normal limits sooner than phosphatase. This explains the fact why phosphatase activity keeps elevated long after the serum bilirubin falls to within normal limits or limits of latent jaundice.

III. Total cholesterol (normal 140 to 200 mg. per cent)

There is a significant drop in total cholesterol level during the acute and the chronic progressive stages, but it returns to normal towards the recovery stage. Total cholesterol was estimated in a few cases, and the results are summarized as follows :—

Stages	Mg. per cent	Number of cases	Percentage
Acute ..	Up to 100	2	12.5
	100-140	13	81.2
	140 and over	1	6.3
Progressive	Up to 100	4	15.2
	100-140	11	42.3
	140 and over	11	42.3
Recovery ..	Up to 100	<i>Nil</i>	<i>Nil</i>
	100-140	7	46.7
	140 and over	8	53.3

Biliary obstruction by itself increases blood cholesterol level, but the effect of obstruction may be modified by the opposite action of either 'infection' or 'cachexia' (Peters and Van Slyke, 1932).

IV. Fractional test meal

A fractional gastric analysis was carried out in a few cases. The presence or absence of bile

in gastric contents did not give any clue as to the existence of obstruction in common bile duct, because 12 cases out of 16 showing clay coloured stools had bile in gastric contents. This fact however indicates that there is partial obstruction to bile flow present in smaller bile canaliculi rather than the common bile duct. There was however evidence of gastritis.

B. Tests not depending on excretion of bile

I. Deamination function of liver

Estimation of amino nitrogen would be the appropriate method of assessing the deamination function. Instead non-protein nitrogen (n.p.n.) was estimated, being the nearest approach (urea and amino-acid nitrogen are the only two constituents of the n.p.n. that can alter the level of the latter markedly, and even considerable alteration of the other constituents, e.g. uric acid, creatine, etc., cannot alter the level to any great extent). Since the blood urea levels have consistently been found to lie within normal limits, the marked fluctuation of the n.p.n. is attributable to the amino-acid level.

The results of n.p.n. estimations may be summarized as follows :—

Stages	Mg. per cent	Number of cases	Percentage
Acute ..	Up to 50	7	29.1
	50-100	12	50.0
	100-150	2	8.3
	150-200	3	12.5
	200 and over	Nil	Nil
Progressive	Up to 50	11	39.5
	50-100	6	19.3
	100-150	4	12.9
	150-200	10	32.2
	200 and over	4	12.9
Recovery ..	Up to 50	23	59.0
	50-100	10	25.6
	100-150	6	15.4
	150 and over	Nil	Nil

Out of the 22 cases that excreted amino-acid crystals the majority of them gave a high n.p.n. level. A significant observation with regard to the n.p.n. level was its marked fluctuation in the same individual at frequent intervals, presumably, amino-acid crystals were excreted every time the n.p.n. level reached a particular high level. Also both urea and n.p.n. were estimated concurrently, and it was noticed that a high n.p.n. level was accompanied by a correspondingly low level of urea.

II. Detoxication function of liver, hippuric acid synthesis (oral method)

Hippuric acid test (oral method) was done in a few cases on the lines suggested by Quick

(1939). The results may be summarized as follows :—

Stages	Gm.	Number of cases	Percentage
Acute ..	0.0-2.0	14	73.6
	2.0-2.5	3	15.8
	2.5-3.0	1	5.2
	3.0 and over	1	5.2
Progressive	0.0-2.0	14	41.2
	2.0-2.5	10	29.6
	2.5-3.0	6	20.6
	3.0 and over	3	19.4
Recovery ..	0.0-2.0	1	5.0
	2.0-2.5	10	50.0
	2.5-3.0	6	30.0
	3.0 and over	3	15.0

The significance of this test is dependent on two factors : (a) Normal absorption of sodium benzoate through the bowel and (b) excretion of urine in normal amounts.

Some cases show oliguria in the early stages of the disease with the result that maximum opportunity for excretion of hippuric acid is not available, consequently smaller amounts of hippuric acid are excreted depending on the volume of urine passed in 24 hours. Hence cases of colitis and oliguria are considered unsuitable for the oral test.

Also, some cases showed toxic symptoms, such as nausea, vomiting, headache, reeling of head, etc., but these did not interfere with the test.

The results have been variously interpreted as follows :—

Impaired liver function 2 gm. and below.

Moderate improvement 2.0 to 2.5 gm.

Marked improvement 2.5 to 3.0 gm.

Normal 3.0 and over.

III. Glycogenic function of liver

(a) Lævulose tolerance test.

(b) Galactose urinary tolerance test.

(a) Lævulose tolerance test (L.T.T.)

Normally fructose reaches a concentration of 20 mg. within the first hour and falls below 8 mg. at the end of the second hour. Lævulose tolerance test was carried out in 11 cases. Definite impairment of liver function was observed in all cases in the chronic progressive stage. Normal curves were however obtained in the recovery stage. L.T.T. did not give any help in recognition of cases of minor degree of damage since normal curves were obtained in some cases with definite active signs, such as tenderness of liver, tinge of jaundice, etc. The L.T.T. however is useful to study the progress of disease.

(b) Galactose urinary tolerance test (G.T.T.)

Galactose urinary tolerance test could be done only on one case due to lack of galactose; and in this case 4.27 gm. of galactose were recovered from urine (normal 0 to 3 gm.).

Blood calcium and phosphorus

Delayed coagulation of blood in jaundice was attributed to deficiency of calcium, as a few cases of jaundice gave lower values. Owing to reciprocal relation between calcium and phosphorus, both these constituents were estimated in 31 cases. Calcium gave an average of 10.6 mg. with extremes of 12.2 and 8.3 mg., while phosphorus gave an average of 3.6 mg. with extremes of 4.9 and 3.1 mg.

PART II—MISCELLANEOUS

Paul-Bunnel test

Paul-Bunnel test was carried out in 45 cases adopting Davidsohn's technique. No cases received serum treatment before and so absorption tests were not considered necessary. The results of Paul-Bunnel test may be summarized as follows :—

Cells	1 : 10	1 : 20	1 : 40	1 : 80	1 : 160	1 : 320
Sheep ..	19	Nil	16	3	5	Nil
Beef ..	18	2	19	5	1	Nil

It was considered that the titre obtained in a few cases was too low to have any diagnostic significance.*

Diastatic index

In view of the relation of the pancreatic enzymes and bile with regard to digestion and absorption of food, it is considered worth while to eliminate any lesion connected with pancreas. In 30 cases, an average diastatic index of 26.9 units with extremes of 30 and 10 were obtained.

Wassermann and Kahn

Serum reaction was carried out in a few cases to eliminate any syphilitic affection of liver, but found to be negative for syphilis.†

DIAGNOSIS

Diagnosis is easy in an epidemic. It is however important that diagnosis be made in the acute or pre-icteric stage in sporadic cases. The cases fall into three groups, from the study of symptoms in the present series :

- A. Febrile group.
- B. Abdominal group.
- C. Mixed group.

* Diagnosis of glandular fever will be justified in 8 cases.—EDITOR, I.M.G.

† False positive W.R. is known to occur in jaundice and much that is written about syphilitic jaundice may refer to 'catarrhal jaundice' with false positive W.R.—EDITOR, I.M.G.

A. *Febrile group.*—Symptoms are similar to either influenza or sandfly fever. The duration of the fever is short, 3 to 5 days, and accompanied by headache and chilly feeling. Eyes look suffused and conjunctiva often injected. Urobilinogen invariably and bile salts sometimes appear in urine before the onset of icterus.

B. *Abdominal group.*—This appears either as 'gastric' or as 'hepatic' type. In gastric type, epigastric discomfort and fullness of stomach accompanied by anorexia are the predominant features. Anorexia sometimes is so distressing that the patient refuses all nourishment. Nausea and vomiting are frequently present. In hepatic type, pain and tenderness over the right hypochondrium with a feeling of tightness in the upper abdomen are present. Nausea unaccompanied by vomiting is very often present in this type. The pre-icteric period in this group is slightly longer, 5 to 7 days. In fact the febrile period merges into the abdominal group.

C. *Mixed group.*—Symptoms are often atypical. Sometimes febrile and abdominal symptoms are present at the same time. The disease commences with hyperpyrexia, or intense headache, or epistaxis accompanied by pain and tenderness of liver, sometimes associated with nausea and anorexia. Cases with a prolonged pre-icteric period are preceded by a feeling of abdominal discomfort long before the enlargement of liver could be made out.

Increased urobilinogen, presence of bile salts, intense anorexia, pain and tenderness, if not a feeling of discomfort in liver area, suggest infective hepatitis. Hippuric acid synthesis is very helpful as it indicates early impairment very often, although normal results may be obtained in the acute stage.

PROGNOSIS

Prognosis is usually good. In the present series there was no fatal case, all the cases including the four that showed cholæmic symptoms had an uneventful recovery. Relapses are not uncommon. Out of 60 cases reviewed 3 cases were relapses within a year.

In the absence of laboratory confirmatory tests it is however difficult to ascertain whether a case is cured or not. The following points may be taken as a guide to assess the amount of residual lesion present after all jaundice had disappeared :—

1. Absence of subjective symptoms for fortnight.
2. Complete recession of liver to its normal size.
3. Absence of pain or tenderness in the hepatic area.
4. Cessation of any recurrent hæmorrhagic diathesis previously present, such as epistaxis, or bleeding per rectum.

The following tests may be considered confirmatory :—

1. Absence of bile salts from urine—these are present long after the jaundice disappears.

2. Van den Bergh should lie within normal limits. It often lies within limits of latent jaundice for a long time after jaundice has disappeared.

3. Phosphatase activity is a very sensitive indicator of any residual lesion, and does not lie within normal limits till complete cure is obtained.

4. Cholesterol should return to normal limits.

It should be borne in mind that van den Bergh comes to lie within normal limits, long before phosphatase activity returns to normal value, and both the tests should be carried out concurrently to obtain a clear idea of the trend of disease.

CONCLUSION

1. An arbitrary but useful classification of infective hepatitis is suggested, acute or pre-icteric, progressive or icteric, and recovery or post-icteric stages, although each stage imperceptibly merges to the next stage.

2. Cases with high n.p.n. level (amino-acid level) excreting amino-acid crystals in urine are mentioned; this being due to either acute atrophy of liver not giving rise to severe clinical symptoms or as a characteristic feature of this disease.

3. Phosphatase activity is considered a very sensitive indicator of any residual lesion; and probably many relapses were cases discharged from hospital before a complete cure, and which could have been identified by estimating phosphatase activity.

4. A low cholesterol content in the acute and chronic progressive stages, reaching normal level in the recovery stage, is often helpful in studying the trend of disease.

5. Van den Bergh was not helpful either in indicating a cure or in localizing the lesion. Serum bilirubin often remains in the latent jaundice limits, that it often helps to study the progress of the disease.

6. Hippuric acid synthesis and the lævulose tolerance tests are very helpful not only to study the progress of the disease, but also to indicate roughly the recovery period; and hippuric acid is more sensitive in indicating minor damage than L.T.T.

SUMMARY

1. Sixty cases of infective hepatitis are reviewed, occurring as an epidemic in Burma general hospitals.

2. Biochemical results of urine, stools, blood, F.T.M., etc., are given and their significance explained.

3. The significance of n.p.n., amino-acid crystals, phosphatase activity, cholesterol, etc., are discussed.

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AMINO-ACID CRYSTALS IN URINE*

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VARIOUS writers have described in various ways, the amino-acid crystals sometimes present in normal and pathological urine, and it often confuses students of clinical medicine with regard to their structure, under a microscope.

* This investigation was carried out while the author was attached to the Central Military Pathological Laboratory of India, Poona.

The following observations are intended to clarify the doubts that may arise specifically in connection with tyrosine and leucine—the two amino-acid crystals that are often mentioned to be present in urine. It should be emphasized at the outset that tyrosine and leucine crystals cannot normally be obtained from urine unless urine is concentrated after precipitating the urea and proteins, if present. It should be further mentioned that the appearance of tyrosine and leucine need not necessarily signify total degeneration of liver or total breakdown of tissues of the body as is generally understood. The following technique has been adopted to obtain the crystals from urines of cases suffering from infective hepatitis.

To a beaker containing 100 cc. of urine about a gramme of lead acetate is added to precipitate the proteins, if present. The urine is then filtered once (or twice, if necessary to obtain a clear filtrate). The filtrate is concentrated by simmering (not boiling) to a syrupy consistency. The urine is then alkalized with ammonia till it is just alkaline to litmus, and rectified spirit is added in order to precipitate urea. The urine is again filtered till it is clear. The final clear filtrate is transferred to a test tube and kept in boiling water. The urine in the test tube is thereby further concentrated till a precipitate forms and settles down to the bottom. This precipitate which contains the tyrosine and leucine is allowed to settle down to the bottom and is spread on a slide.

These crystals were isolated in 22 out of 60 cases of infective hepatitis. It may be mentioned in this connection that the cases of infective hepatitis from which the crystals were isolated did not appear to be any different from the rest except that the disease was protracted and convalescence delayed. It is possible a mild degree of liver necrosis or atrophy was present.

Leucine.—Leucine crystals are represented by Cameron (1942) as hexagonal and colourless crystals, but it is not always that crystals of such shape are isolated. Hawk and Bergeim (1939) gives an impression quite different from that of Cameron (1942), while Harrison (1937) gives an illustration completely different from those of Cameron and Hawk, and Bergeim. It only needs to be mentioned that leucine appears in various forms as represented in the photomicrographs. In figure 1, plate XXIX, these forms of leucine crystals may be differentiated and are arbitrarily classified as 'impure', 'transitional', and 'pure' forms of leucine. In the photomicrograph, arrow points to the 'impure' form of leucine. These forms are roughly circular in shape and of various sizes. The whole crystal is smudged with amorphous precipitates thereby obliterating the radial striations which can however be made

out at the periphery. A thin rim is present round each crystal, but it is not evident except in the 'transitional' or the almost 'pure' forms.

The arrow 2 points to the 'pure' form (or more correctly, the almost pure form) of the leucine crystal. These appear in the photomicrograph like 'cogwheel' and the thin transparent rim is definitely marked out. Each rib of the cogwheel represents one of the sides of the 'hexagonal transparent crystals' which Cameron (1942) describes. Being transparent, the hexagonal nature of the crystals is not well marked. They are of course easily evident as hexagonal, transparent and circular when the cogwheel like crystals are broken down.

The 'transitional' form is represented in the same plate and marked by arrow 3 and forms an intermediary to the 'impure' and the 'pure' forms.

Tyrosine.—Most of the writers agree that tyrosine crystals are yellow and appear like sheaves, but they are often confused with acid sodium urate or calcium urate and rarely with calcium oxalate. In the present series, two forms of tyrosine are differentiated, namely 'sheaves' type and the 'puff ball' type.

The 'sheaves' type resembles the acid sodium urate as indicated in figure 2, plate XXIX, along with the tyrosine crystals, from which they are marked out by the arrows. The differentiation between the sheaves type of tyrosine and acid sodium urate crystals is made out by the fact that in the former the radiations are thin, slender and needle-like, while those of the latter appear like thick prismatic crystals. Tyrosine crystals are yellow, while acid sodium urate are colourless invariably.

Figure 3, plate XXIX, represents the 'puff ball' type and gives a clear idea of the radial striations of the crystal and observed in a higher magnification ($\times 400$); and figure 5, plate XXIX, represents the thick prismatic needles of acid sodium urate, so often mistaken for tyrosine.

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AUREOMYCIN IN TYPHOID FEVER***A PRELIMINARY REPORT OF CLINICAL TRIAL
IN FOUR CASES**

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AUREOMYCIN is a new antibiotic discovered by Duggar (1948) from a strain of streptomycetes. It has a remarkable range of activity, acting

two cases. The findings were thus equivocal. However, it was felt that some benefit was obtained since, soon after aureomycin therapy, blood, stool and urine cultures became negative. Large oral doses may be required.

With a limited supply of the drug at our disposal, it was decided to try out large oral doses of aureomycin in typhoid fever at the Clinical Investigation Ward of the K. E. M. Hospital, Parel.

The drug was tried in 4 adults, one female and 3 males, all being proved blood culture positive cases. Two dosage schedules were tried :—

		Vi phage	Dosage schedule	Duration of treatment	Total dose	Day of disease on which treatment was started
Schedule 1	Case 1	Type A	0.25 g. one-hourly for 3 hours 0.25 g. two-hourly for first 24 hours. 0.25 g. four-hourly	10 days	32 g.	19th
Schedule 2	Case 2	Type A	1 g. one-hourly for 3 hours	6 days	47 g.	18th
	Case 3	Type A	1 g. two-hourly for first 24 hours, later 1 g. three-hourly.	5 days	45 g.	14th
	Case 4	Untypable	Same as above but 0.75 g. three-hourly from 4th to 6th day.	6 days	50 g.	12th

against many Gram positive and negative organisms (Bryer *et al.*, 1948; Finland *et al.*, 1948) and against the rickettsiae and certain viruses (Angstein *et al.*, 1948; Dowling *et al.*, 1948; Ross *et al.*, 1948; Schoenbach *et al.*, 1948; Wong and Cox, 1948).

Aureomycin has been found to exert a favourable influence in the salmonella infections of the gut, inhibiting most Gram-negative bacilli including typhoid and the other salmonella species in a concentration of 25 g. of aureomycin per ml. serum or less (Finland *et al.*, 1948).

In September 1948, Bryer and his co-workers treated two cases of typhoid fever with aureomycin with favourable initial response. Three early cases of typhoid fever treated with aureomycin in daily dosage of 60 to 100 mg./kg. per day by mouth and 3.5 mg./kg. per day parenterally resulted in negative blood and stool cultures within 48 to 72 hours. The clinical response varied, however, with defervescence occurring in 24 hours, 8 days and 11 days respectively (Schoenbach *et al.*, 1948).

Finland *et al.* (1948) treated 5 cases of typhoid fever with aureomycin. The results were good in one, doubtful in two and failed in

It will be noticed that 3 cases suffered from a Vi phage type A variety of *S. typhi* infection and in one case the organism was untypable. The average duration of treatment in group II was 5.66 days. In two cases, the treatment was started during the third week of illness; in two other cases, during the second week. The cultural examination of blood was repeated 48 hours and 5 days after initiation of therapy. The stool and urine cultures were done during convalescence and repeated 7 to 10 days later.

The case summaries are given below :—

Case 1.—P. T., female, 20 years, was admitted on 2nd April, 1949, with a history of continuous fever for 15 days. The onset was gradual, with a fluctuating temperature for first 10 days. For the previous 5 days, fever was continuous. The patient had suffered from chorea 4 to 6 years previously; and had been keeping indifferent health for the last 2 years. There was no history of contact nor of T.A.B. inoculation. Meals were taken at home. A cousin of hers had suffered from typhoid 3 years previously. On admission, the patient had a temperature of 99°F., pulse rate was 120 per minute and respiration rate was 30 per minute. She complained of intense headache, cough, generalized bodyache, abdominal discomfort and anorexia. The conjunctivae and throat were congested and the tongue was

* Based on a report submitted to the Therapeutic Trials Committee of Indian Research Fund Association.

centrally coated with a red tip and red margins. She was fairly well built and nourished but in a severely toxæmic state. Physical examination did not reveal any positive findings except that the spleen was just palpable. Blood pressure was 120/80 mm. Hg. The urinalysis showed a trace of albumin, a few red cells and pus cells. The total leucocyte count was 8,750 per c.mm. Neutrophils 70 per cent, lymphocytes 29 per cent and large mononuclears 1 per cent, *S. typhi* (Vi phage type A) was isolated, on cultural examination of the blood. Electrocardiogram tracing was normal.

The patient was given aureomycin therapy orally (on 6th April, 1949). The dosage is given in the table. The blood culture was repeated 5 and 7 days later. The first culture gave a growth of *S. typhi* but the second was negative. The temperature touched normal on the third day of treatment but again rose, and ran an intermittent course before finally settling down on the 13th day after starting aureomycin therapy.

It was felt that aureomycin did exert a beneficial though slight effect with the dosage employed.

Case 2.—V. K. G., male, 15 years, student, was admitted on 20th April, 1949, with a history of continuous fever for 6 days. Following malaise for 2 to 3 days, the onset of fever was gradual. There was a history of having suffered from typhoid fever 1½ years previously. There was no history of contact or of T.A.B. inoculation. The meals were taken at a hotel. Among the prominent symptoms at the onset were headache and anorexia. He was admitted in a severely toxæmic condition with a heavy central coating on the tongue, congested pharynx and rose spots on the trunk. The temperature was 101°F., pulse 98 per minute and respirations 32 per minute. Both liver and spleen were one finger palpable and rhonchi were present in both the lungs. The chest was clear on screening.

The total leucocyte count was 2,250 cells per c.mm., neutrophils 56 per cent, lymphocytes 43 per cent, and large mononuclears 1 per cent. No malarial parasites were detected. The blood culture gave a growth of *S. typhi*—Vi phage type A. Urinalysis showed albumin (++) , a few red cells, pus cells and granular casts.

On the 24th and 27th April, type specific anti-Vi phage was given intravenously with no particular benefit except that the toxæmia was reduced. The blood culture was still positive and *S. typhi* had practically lost their Vi antigen. So on 2nd May aureomycin was started by mouth (for dosage see table). The temperature gradually came down to normal on the third day but rose once more as soon as the treatment was discontinued. It pursued a remittent course for about a week before finally settling down. No toxic reactions of the drug were observed. The blood cultures taken at the end of second and seventh days of therapy did not show any

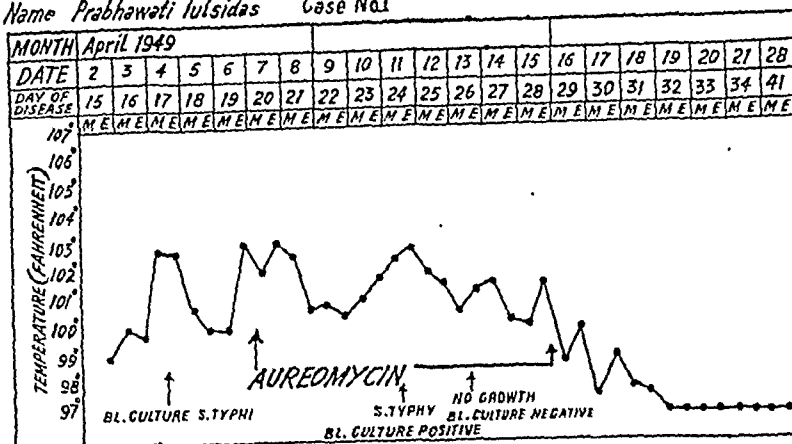
growth of organisms. The urine culture showed a growth of *E. coli* but the second culture was negative. It was concluded that aureomycin did exert a favourable influence on the course of the fever.

Case 3.—R. A., male, 28 years, watchman, was admitted on 20th April, 1949, with a history of continuous fever for 10 days. The onset was fairly sudden without a rigor. The fever gradually increased and finally became continuous. No history of contact or of T.A.B. inoculation was available. On admission, the patient complained of headache, anorexia and pain in the abdomen and in a moderately toxæmic condition. He had a slow pulse, a coated tongue and a moderate degree of abdominal distension. Liver and spleen were not palpable. The chest was clear on fluoroscopic examination. The total leucocyte count was 3,359 c.mm., neutrophils 24 per cent and lymphocytes 76 per cent. Malarial parasites were not detected. *S. typhi* of Vi phage type A were recovered from the blood. The urinalysis was normal. On 2nd May, the patient was put on oral aureomycin therapy. The dosage employed was the same as for case 2 (see table), 12 g. were given on the first day and 8 g. daily subsequently. From 4th May (i.e. on 3rd day of therapy) the temperature started subsiding rapidly and touched normal in 2 days more. On 7th, the day on which aureomycin therapy was concluded, the temperature remained normal. As soon as aureomycin was stopped, the temperature started rising gradually, returning to normal after a further 7 days. The blood culture repeated at the end of second and seventh days were negative. The stool and urine culture examinations made during the convalescence were negative.

In this case, aureomycin definitely exerted a beneficial effect, blood cultures becoming negative in 48 hours. Clinical recovery occurred on the 8th day. Probably had the drug been continued for a few days longer the pyrexial period of 7 days would not have occurred.

Case 4.—S. N., male, 28 years, mill hand, was admitted on 8th May, 1949, with a history of continuous fever for 8 days. The onset was rapid with a feeling of chilliness. Since then high continuous temperature had been maintained. He had developed a cough in the last 24 hours and had 2 to 3 stools just before admission. There was no history of contact or of T.A.B. inoculation. He also complained of headache, anorexia and slight distension of the abdomen. He was in a severely toxæmic state almost verging on semi-consciousness, had a centrally coated tongue and congested pharynx. Rhonchi were present in both the lungs and the spleen was two fingers palpable. No rash was seen. The total W.B.C. count was 4,900 cells per c.mm. with neutrophils 89 per cent and lymphocytes 11 per cent. Malarial parasites

Name Prabhawati Tulsidas Case No I



Name Vasant Kúsul Giri Case No. 22

MONTH	April 1949																																													
DATE	20	21	22	23	24	25	26	27	28	29	30	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31				
DAY OF DISEASE	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48			
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F

TEMPERATURE (FAHRENHEIT)

107
106
105
104
103
102
101
100
99
98
97

↑ S TYPHI
BL CULTURE POSITIVE

↓ S TYPHI
BL CULTURE POSITIVE

← AUREOMYCIN 47.5 G →

STOOL CULTURE
NO PATHOGENS
URINE CULTURE E. COLI

STOOL CULTURE
AND URINE
CULTURE
NO PATHOGENS

MONTH April 1949										MAY																			
DATE	26	27	28	29	30	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	26	27	28	29	30	31			
DAY OF DISEASE	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	1	2			
	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E			

TEMPERATURE (FAHRENHEIT)

AUREOMYCIN
45 G

NO GROWTH
BL. CULTURE NEGATIVE

STOOL CULTURE
URINE CULTURE } NEGATIVE
ON 21-30
A 30-31

BL. CULTURE - S. TYPHI
POSITIVE

NO GROWTH
BL. CULTURE NEGATIVE

MONTH	May 1949																																												
DATE	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	1	2	3	4	5	6	7															
DAY OF DISEASE	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38															
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were not detected, *S. typhi* of Vi phage type A were isolated from the blood.

On 12th May, the patient was put on aureomycin given by mouth. The dosage schedule is given in the table. The treatment was over on the 18th May and a total of 50 g. aureomycin was given. On the 6th day of aureomycin therapy, his temperature started fluctuating and remained normal for many hours on the 7th day. As soon as aureomycin was omitted the temperature rose, finally settling down after 10 days. The blood cultures repeated at the end of two days' therapy showed *S. typhi* but the subsequent cultures were negative. No pathogens were grown on repeated stool culture examinations during the convalescence. The first urine culture during convalescence gave a growth of *E. coli*. No toxic reactions were observed nor were any changes observed in the leucocyte count. It was felt that the continuation of the therapy for a couple of days more would have given a better result.

Reviewing all the four cases together it appears that the blood cultures become negative in about 48 to 72 hours following aureomycin therapy when large oral doses are used. This confirms the findings of Schoenbach and his co-workers in 1948. The clinical recovery however was not striking, the temperature settling down after 7 to 10 days. The course of the disease was definitely made milder and no complications developed. All the four cases, which were in a severely toxæmic state on admission, survived. The only toxic reactions of the drug observed were a transient anorexia, nausea and a slight looseness of the bowel.

Summary

Four cases of culture positive typhoid fever which were treated with aureomycin with beneficial results are reported. The drug deserves further trials.

We take this opportunity of thanking the Dean, King Edward Memorial Hospital, Bombay, for facilities, Lederle Laboratories (India) Ltd., for supplies of aureomycin, and Indian Research Fund Association for permission to publish this paper.

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ERRATA

A STUDY IN BENGALEE AND BEHAREE FEMALE PELVIS BY ROENTGEN-PELVIMETRIC METHOD

A Preliminary Communication

By N. C. SEN, M.B. (Cal.), F.R.C.S. (Edin.), D.G.O. (Dub.)
Obstetrician and Gynaecologist, Sanctoria Hospital, Disergarh P. O.

In the above article published in the *Indian Medical Gazette*, August 1949, page 339, column 2, table I, column 4, items 3 and 4

for 4.4 read 22.7

for 22.7 read 4.4

A Mirror of Hospital Practice

A CASE OF MYASTHENIA GRAVIS

By M. HATANGDI, M.B., B.S., D.T.M.
Lady Jackson Hospital, Dohad

A. U., an elderly Muslim male, aged 50 years, an armature winder of the electric department, was admitted to the hospital on 30th May, 1949, for investigation.

The history was that for the last 18 months he had been noticing an increasing degree of weakness and tiredness of the upper eyelids and the shoulders. This weakness started first in the right upper eyelid and later on spread on to the left eyelid and subsequently to the shoulders. On admission the symptoms were felt more in the right upper eyelid and the left shoulder. He would start the day well but as it wore on, the eyelids would start drooping down gradually and it required an ever-increasing effort to keep the eyes open; finally he had to tilt the head back and see with downward slanting vision when effort could no longer overcome the ptosis. At first he used to see 'double' but now the diplopia has disappeared. His co-workers used to remark about his 'falling asleep while at work'. Sometime later he noted that the shoulders, particularly the left one, would start aching and drooping down and a feeling of fatigue and weakness would make it increasingly difficult to lift the shoulders and use the arms. Early in the day he could brace up the shoulders with slight effort but towards the end they would droop down in spite of all efforts and the feeling of weakness in the upper extremities would make it very difficult for him even to shake hands with people.

He complained of slight general weakness and lassitude but the areas of marked weakness were strictly and definitely localized. One thing he had learnt by experience, was that these symptoms of 'fatigue paralysis' came on after he had been at work for some time and that they tended to disappear on rest—the longer the period of rest the more refreshed and energetic would he feel. He had reported sick previously too, but the true cause was missed and he was treated for eye strain with glasses, for general debility with tonics and for neuralgia with vitamin B₁ and vitamin B complex—all with doubtful relief. The thing that brought him to this hospital was a rather sudden onset of weakness of the lower jaw four days previously. He felt a rapidly increasing difficulty in chewing betel leaf as was his wont after meals, and in swallowing it. His friends and relatives had remarked that during conversation, after a while, his speech would get slow, slurred and indistinct and he himself would find the tongue too heavy to articulate and talk freely.

Excepting the betel leaf he had no addictions. There was no history or evidence of any specific disease nor of any illness that usually cause central or peripheral nervous diseases. There was no history of any neuro or myopathic disabilities in the family on either side.

On examination there was no evidence of any endocrine disorder or persistent thymus. The general build and health were good, and the pulse and blood pressure were normal.

Barring a slight intention tremor of the left hand, nothing abnormal was noted in the nervous and muscular systems. The occurrence of 'fatigue paralysis' of the muscles of the eyelids, the tongue, deglutition and shoulders was confirmed by simple tests evolved to tire out the particular muscles concerned. Thus the ptosis, dysarthria, dysphagia, etc., were all found to be genuine. It was also noted that prolonged rest caused these paralytic symptoms to disappear. In fact as the patient himself remarked he had not felt so refreshed and energetic as in the hospital for some months; evidently the enforced rest was beneficial, routine urine examination revealed no abnormality. Though no Kahn or Wassermann test was done due to lack of facilities and electrical reactions could not be done, the clinical findings were deemed sufficiently characteristic to warrant the diagnosis of myasthenia gravis.

He was given orally as well as parenterally physostigmine salicylate in full dosage combined with ephedrine and atropine as a therapeutic test—but with disappointingly little effect. However the test was repeated with a prostigmin injection, resulting in a dramatic confirmation of the clinical diagnosis. All the symptoms of 'fatigue paralysis', which had been intentionally brought on before the injection, disappeared as if by magic within a few minutes of the administration of the drug.

He was duly discharged and advised further treatment with prostigmin, in conjunction with ephedrine and atropine, at home and to come for periodical observation as an out-patient. When seen a few days ago he seemed quite happy and normal and said that he no longer had the old symptoms.

I am grateful to the Chief Medical Officer and the District Medical Officer, Dohad, B. B. & C. I. Railway, for permission to report the above case.

A CASE OF AMOEBIC VAGINITIS

By M. BALASUBRAHIMANYAN, M.D.

and

OMANA CHERIYAN, M.B., B.S.

Departments of Pathology and Gynaecology, Christian Medical College Hospital, Vellore

VAGINITIS due to *Entamoeba histolytica* is not common. Sen (1949) mentions that only 14 cases have been reported between the years 1916 and 1948. According to Bickers (1943), infection by *Entamoeba histolytica* accounts for 0.5 per cent of cases of leucorrhoea. Many of the cases reported are from the countries where amoebiasis is prevalent. de Rivas (1944) reported, what he believed to be, the first case in America. In view of the rarity of the condition the following case is reported:

Case report

K., a girl of 12 years, unmarried, was admitted on 22nd June, 1949, with the complaint of blood-stained discharge per vaginam for 6 months. Before the present illness started, she was having blood-stained loose motions for two months and had some treatment in another hospital. She complained of occasional pain in the lower abdomen. The micturition was free and there was no burning during the act. A detailed vaginal examination was not possible since she had not attained puberty and the hymen admitted only one finger. There was blood-stained purulent exudate in the vagina and the cervix was high up. The uterus was small in size and appeared retroverted. There was a small congested area in the posterior vaginal wall about half an inch from the vaginal outlet.

The vaginal discharge was sent for pathological examination and a stained preparation showed epithelial cells and an inflammatory exudate consisting mainly of mononuclear cells and polymorphonuclear leucocytes. There were some large pale staining cells, with indistinct nuclei, resembling amoebae (see figure, plate XXX). A drop of the fresh discharge was obtained from the vagina and examined wet. Besides epithelial cells and inflammatory exudate, there were a large number of red blood cells and trophozoites of *Entamoeba histolytica*. The amoebae were actively motile and contained ingested erythrocytes. Stools examined on three occasions did not show any evidence of infection by *Entamoeba histolytica*.

She was treated with daily intramuscular injections of half a grain of emetine hydrochloride for six days. Locally, saline douches were given and stovarsol vaginal compound tablets introduced into the vagina. At the end of the treatment the vaginal discharge stopped completely.

Discussion

Amoebic vaginitis is characterized by sero-sanguineous or frankly bloody vaginal discharge not responding to ordinary methods of treatment. According to Weinstein and Weed (1948), 70 per cent of the cases show involvement of the cervix. The lesions take the form of shallow punched out ulcers and the uterus is often enlarged and tender. Most of the reported cases were associated with amoebic infection of the intestines. In the case reported by Sen (1949) there was also infection of the lower urinary tract. The condition responds to injections of emetine hydrochloride and local applications of stovarsol vaginal compound.

According to Sen (1949), the spread of infection is helped by the method of ablution practised in Bengal to cleanse the part after defaecation. This applies also to South India where a similar practice is followed.

Our thanks are due to Dr. H. M. Lazarus for her kind permission to report this case.

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UNUSUAL CURE OF ANGINA PECTORIS AFTER VIRUS DISEASE

By K. S. HOSSAIN, M.B.

Patuakhali P. O. (Barisal)

N. C. C., 56, Hindu male, a compounder, had been suffering from attacks of angina pectoris with typical signs and symptoms for the last 3 years. Frequency and duration of attacks had increased during the later part, six months ago, even to the extent of two to three attacks a day, without any appreciable relief by amyl nitrite capsules, which used to abort attacks previously. Laboratory examinations of all sorts, cardiogram, etc., were negative.

About 4 months ago the patient was suddenly attacked with smallpox and recovered uneventfully.

For the last 3 months, after recovery from smallpox, the patient has not had an attack of angina pectoris.

What can possibly be the reason?

A CASE OF EUWING'S TUMOUR

By CAPTAIN G. S. RAO, M.B., B.S. (Andhra)
 Sahur (Vizagapatnam Dist.)

Name and family history.—K., 18 years of age, Kapu, cultivator, belongs to Kottavalsa near Parvatipuram, Visakhapatnam District.

Previous history.—Had extensive burns, leaving scars over right hand and right calf about 2 years ago.

Present history.—He ran to overtake a running cart over a distance of a few yards in the last week of April 1949, and at the close of the run felt a slight but sharp pain at the site of the present swelling. It lasted only for a few minutes. No further pain or swelling was felt subsequently till the first week of June 1949, when a swelling over the upper part of the right thigh was noticed. The swelling gradually increased up to the present dimensions. The only symptom that has been worrying him ever since the swelling appeared is the pain. The pain of late has been very intense and causing sleeplessness.

Physical findings.—A well-nourished young adult. Not anæmic. No œdema over any part of the body. No deformities (except the extensive scar tissue over right hand due to old burns). Walks with slightly flexed hip joint (right side).

C.V.S.	N.A.D.
A.S.	N.A.D.
C.N.S.	N.A.D.

Swelling.—An almost fusiform swelling confined to the upper 1/3 of the thigh. The skin over the swelling is hardened by some blisters applied by the patient at home for the relief of pain. No enlarged veins seen over the surface. The swelling is rather soft and mainly confined to the anterior and lateral aspects of the upper portion of the right femur. It is warm to touch and tender on deep pressure alone on the anterior aspect. Even on this deep pressure it is not tender on the lateral aspect. It is fixed and not movable. No pulsation is felt.

Flexion at the hip joint is limited due to the swelling. Temperature in the evening rises up to 99.4°F. Morning it was 98°F. He was under my observation for five days.

W.B.C. total count: 8,200. P. 68; L. 30; E. 1; M. 1.

Urine.—No sugar; no albumin; no Bence-Jones proteins; phosphates ++++.

The x-ray finding of the tumours—suggestion of Ewing's tumour (see figures 1 and 2, plate XXX).

In view of the rarity of the disease the case is reported. At the outset one is apt to mistake it for an inflammatory condition (abscess); at any rate the writer so mistook it.



Fig. 1.—Brain showing extensive degeneration of white matter and corpus callosum. Cortical portions healthy.



Fig. 2.—Showing junction of healthy cortical and degenerated grey matter and a blood vessel with collaring. (Low power.)

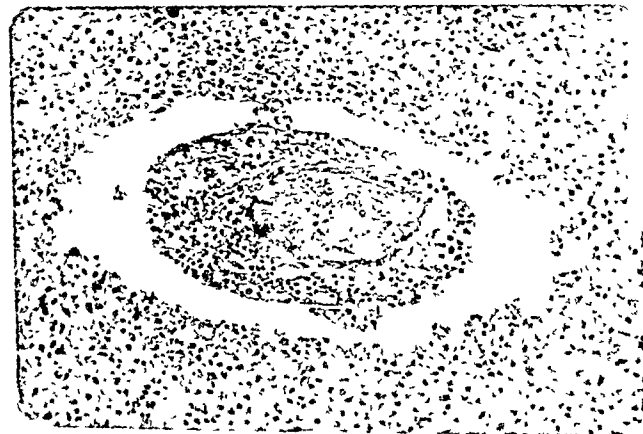


Fig. 3.—Degenerated area only with a blood vessel showing perivascular collaring limited to wall and masses of scavenger cells, mononuclear cells, etc., around the blood vessel. (High power.)

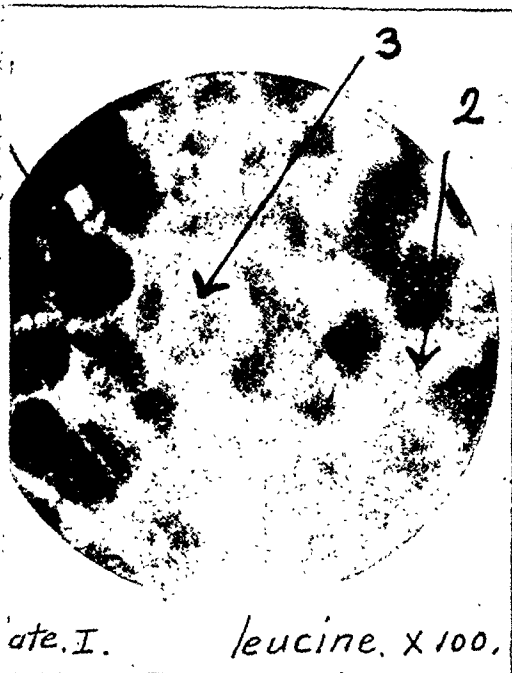


Fig. 1.—Leucine $\times 100$.

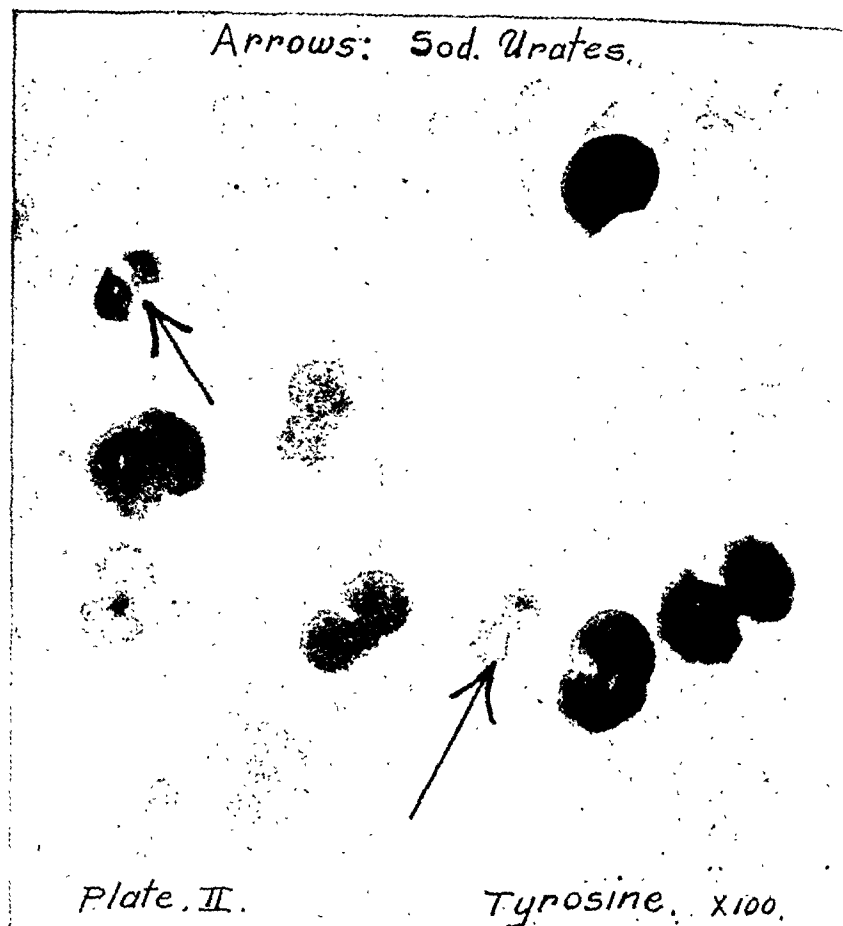


Fig. 2.—Tyrosine $\times 100$.

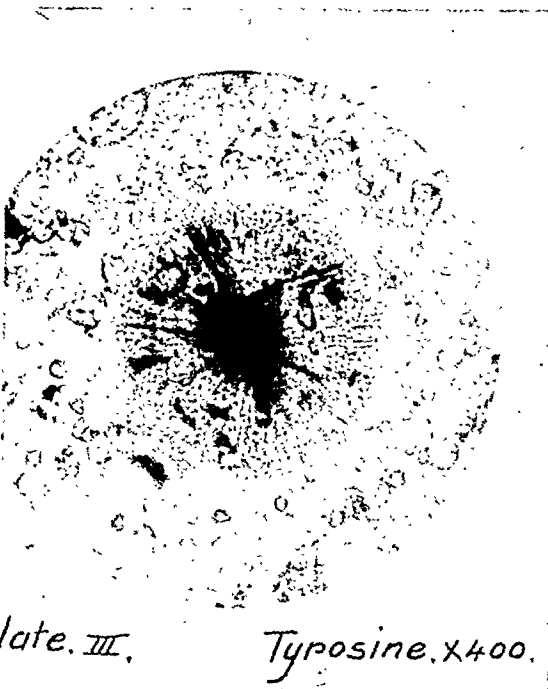


Fig. 3.—Tyrosine $\times 400$.

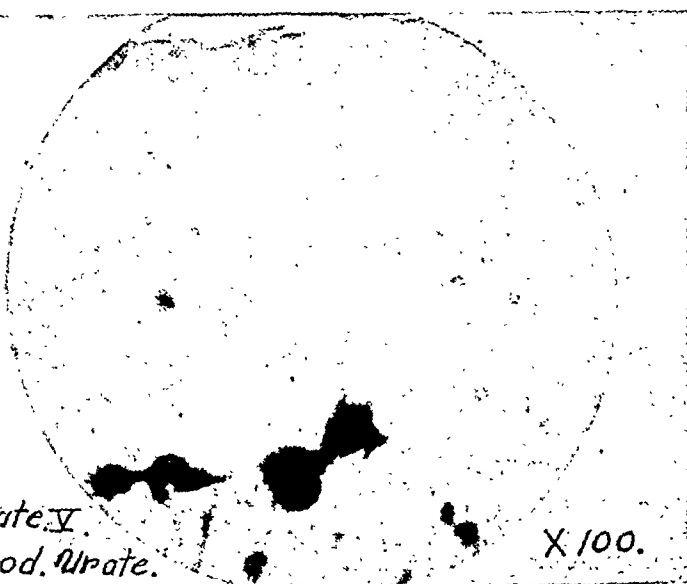


Fig. 5.—Sod. urate $\times 100$.

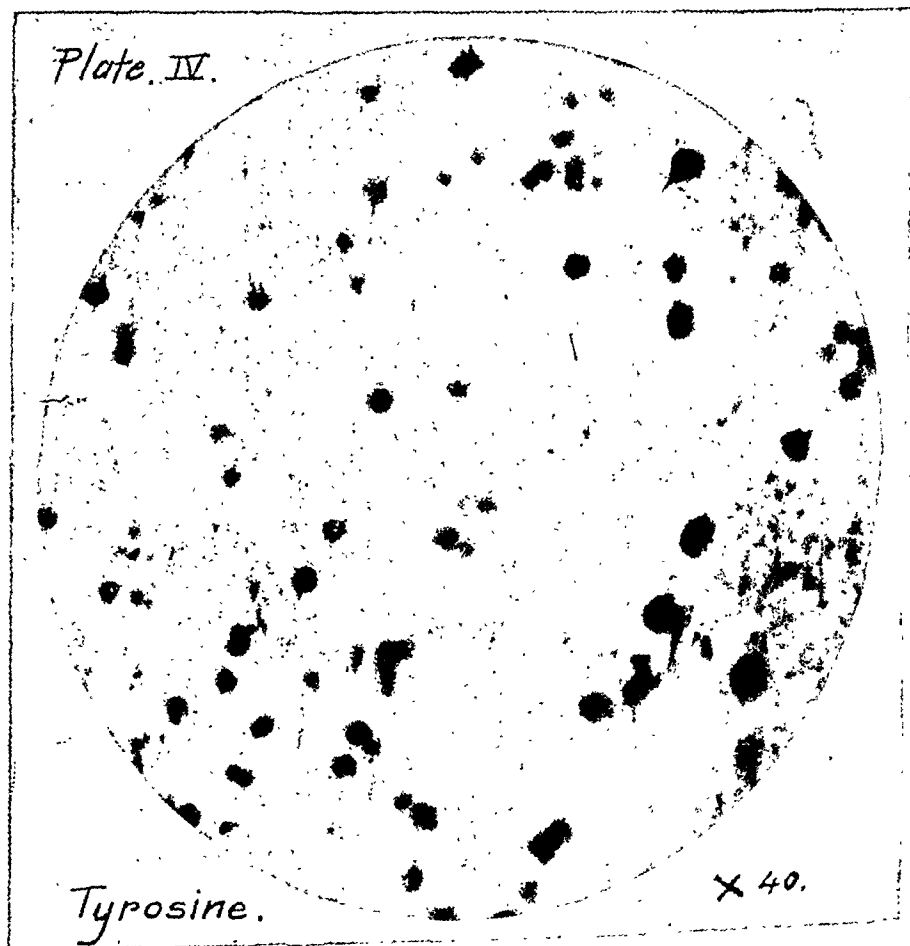


Fig. 4.—Tyrosine $\times 40$.

PLATE XXX

A CASE OF AMŒBIC VAGINITIS M BALASUBRAHMANYAN &
OMANA CHERIYAN. (M H P) PAGE 501



A CASE OF EUWING'S TUMOUR . G. S RAO (M H P) PAGE 502



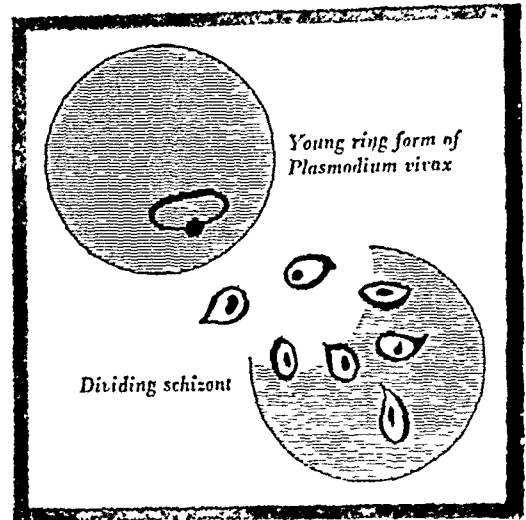
Fig 1



Fig. 2

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the treatment of malaria



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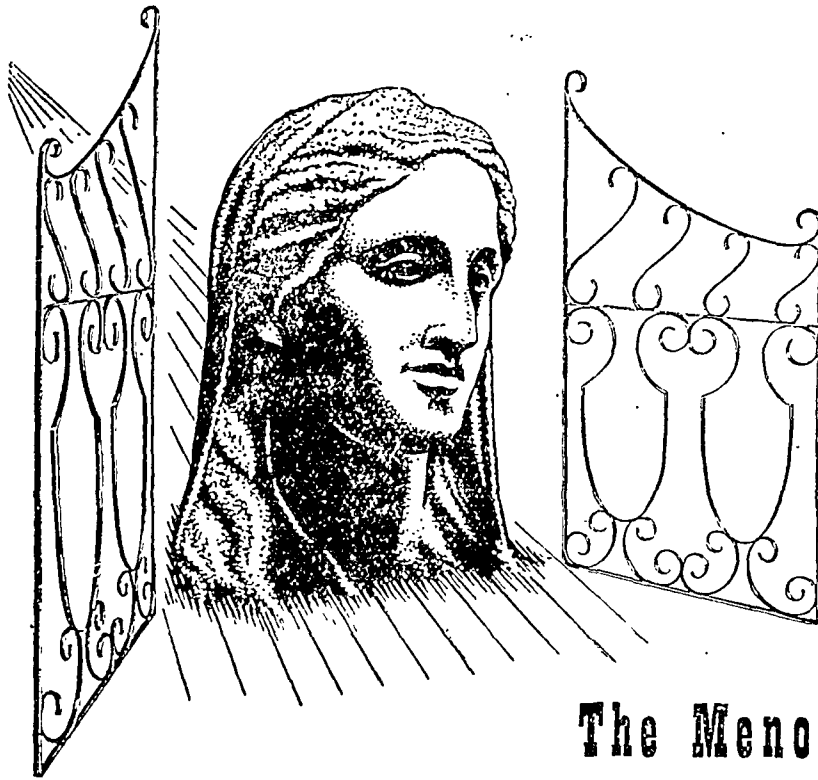
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Indian Medical Gazette

NOVEMBER

HYDROGENATED VEGETABLE OILS: VEGETABLE GHEE

THERE is a world shortage of edible vegetable oils and animal fats. In India the animal fats were never popular with the bulk of the population. The world shortage, therefore, makes the vegetable oils doubly short in India. Oil-yielding nuts are being sent out to improve the trade balances. 'Lac, cashewnuts, raw cotton, raw hides and skins and groundnuts are among other goods which record advance over October's figures' (Daily Press, 1949).

Important edible oils.—Of edible vegetable oils the pride of place goes to the coconut oil, and then comes the groundnut oil an undoubted second. From them are made by clarification or by hydrogenation foodstuffs looking remarkably like clarified butter, the ghee, that much misunderstood commodity so prized by the indigenous population and so despised by the Western sojourners.

Other oils like the mustard oil, sesame oil and olive oil have also become scarce partly by imitation and partly because the have-nots of the pre-World War II days are now demanding and having their full share in the food of the world, beginning with the cheapest and the best known.

Really the groundnut from the pod of *Arachis hypogaea*, the peanut or the 'operation peanut' of the recent British enterprise in Africa (Owen, 1949) provides the oil number one. The plant is an annual and grows quickly, most unlike the coconut. In large-scale production, however, the British East Africa scheme has fared badly. In defeating the government in the House of Lords in the British Parliament on 15th December, 1949 (reported in this delayed issue of the Journal for November 1949) the 'Opposition Peers mentioned that £30 m. sunk in the scheme to increase the world's supply of vegetable oil had been squandered and had produced very few groundnuts' (Daily Press, 1949). The fault, however, does not appear to lie with the groundnuts but with 'the refusal of the auditors to certify that proper accounts have been kept' (Crossman, 1949).

In India the groundnut oil comes mostly from Khandesh, Madras and Hyderabad. Our information obtained by visiting a local vegetable oil ghee factory is that although the quantity is enough, in the quality there is much room for improvement. The defect in quality results mainly from rancidity which results from defective storage of the nut mostly.

Preparation of vegetable ghee.—The coconut oil makes 'cocogem' after filtration only.

Perhaps it is the most acceptable cooking oil when prepared freshly. A faint flavour of the nut is not unpleasant. Between the two world wars the European countries not using much lard or olive oil were replacing their usual cooking medium, the butter, by cocogem.

The groundnut oil is neutralized, decolorized, deodorized, filtered and hydrogenated. The hydrogen in the presence of a catalytic agent (finely divided nickel obtained from nickel formate, for instance) raises its melting point, thus imparting to it the appearance of ghee. The rise in the melting point is controlled by the quantity of the hydrogen mixed with the oil and by the concomitant temperature and pressure. The aim is to keep the melting point between 31°C. and 37°C.

The groundnut oil has no vitamin A of the butter fat, of course, though it has vitamin E not found in the butter fat. The former vitamin is added to it. The vitamins may be obtained from fish oil or may be a synthetic product (for the benefit of the vegetarians) or only carotene (provitamin A) may be added to impart the colour of ghee from butter from cow's milk. Some manufacturers add only vitamin D (the cheapest which entitles them to declare that this product is 'vitaminized'). Diacetyl is sometimes also added to impart a taste of butter: so real is this taste that of two samples of hydrogenated groundnut oil, one with diacetyl and one without, available simultaneously, the rats will only eat the one with the chemical.

The groundnut product is so much like ghee that military establishments call it ghee and call the real stuff *milk ghee*. The trade names of the product are Dalda, Vanaspati, Rasoi Kusum, etc., etc. (some 20 names in India alone and many more in the U.S.A.).

Food value of oils, cocogem, hydrogenated groundnut oil and milk ghee.—In the calorific value there is no difference. In the rate of assimilation there is a difference. Ultimately, however, 97 per cent of all fats and oils are assimilated by the system.

The milk ghee is the one article of diet specially prized by the Punjabis of both the Punjabs. In the good old days when the Punjabi troops remained unsophisticated villagers in the cantonments the subedars used to reconcile disputants by making one party bring ghee for the other on his return from next leave. In both parts of the divided province the difference between a rich man's diet and a poor man's diet is the ghee, quality and quantity thereof. Milk and milk product characterize the diet of the Punjabis and make their expectation of life the highest in India. 'May you have milk cattle in your house and may you have sons' is the benediction given to a bride on her first arrival.

A recent prejudice against vegetable ghee.—About 2 years ago rats and mice fed on vegetable ghee were reported to have lost their fur and

eyesight. We understand that experimental work undertaken at several centres of research, subsequent to the adverse report, has not been able to build a case against the vegetable ghee.

Adulteration of milk ghee by vegetable ghee.—This undoubtedly occurs. The vegetable ghee can even be incorporated into butter by adding the former to the milk. The detection though possible (by determining volatile fatty acid by Reichert-Polenske process) is laborious. It was suggested that some colouring matter should be added to the vegetable ghee. This suggestion has been withdrawn. Now sesame oil is added to the extent of 5 per cent. This quantity can be detected easily by a colour test.

Specification laid down for the vegetable ghee.—A government notification (Notification, 1947) lays down the following :

The Vegetable Oil Products Controller for India hereby prohibits the manufacture, stock or sale of any vegetable oil product, which does not conform to the following particulars, namely :—

1. It shall not contain any harmful colouring, flavouring or any other matter deleterious to health.
2. It shall not have moisture exceeding 0.25 per cent.
3. The melting point as estimated by the capillary slip method (as described in Note 1 below) shall be from 31°C. to 37°C. both inclusive with a tolerance of 2°C. on either side.
4. The butyro refractometer reading at 40°C. shall not be less than 48.0.
5. It shall not have unsaponifiable matter exceeding 1.5 per cent.
6. It shall not have free fatty acids calculated as oleic acid exceeding 0.25 per cent.
7. Diacetyl, if present, shall not be in excess of six parts per million.
8. The product on melting shall be clear in appearance. Its taste shall be free from staleness or rancidity.
9. On and after the 1st March, 1947, it shall contain refined or refined hydrogenated sesame (til) oil not less than 5 per cent by weight so that when the vegetable oil product is mixed with refined groundnut oil in the proportions of 20 : 80, the red colour produced by the Baudouin test (as described in Note 2 below) shall not be lighter than 2.0 units in a 1 cm. cell of a Lovibond scale.

Note 1.—The 'Capillary Slip Method' is as follows :—

- (i) Thin walled glass tube, open at both ends with an external diameter of 1.2 to 1.5 mm. and internal diameter of 0.83 to 1.1 mm. and length 5 to 6 cm., should be used after proper cleansing and drying.
- (ii) The sample of fat should be completely melted and well mixed at a temperature of about 50°C. Insert the capillary tube so that a column of fat about 1 cm. long is forced into it. Allow the fat in the tube to just set by keeping the tube in a horizontal position during winter, and during summer the tube may be put on a perforated metal tray which is so placed inside a small water bath containing water at 15°C. to 17°C. that the bottom of the tray just touches the water.
- (iii) The tube is then placed in a test-tube immersed in water at 15°C. to 17°C. for one hour.
- (iv) Suspend a thermometer (reading in 1/5th of a degree) in the centre of a beaker of water at 10°C. (the beaker is to be provided with a side tube heating arrangement) so that the

lower end of the fat column is 3 cm. below the surface of water. Heat the side tube of the apparatus gently, so that the temperature of water increases slowly at the rate of 2°C. per minute till the temperature reaches 25°C. and thereafter at the rate of 1/2 a degree per minute.

- (v) Note the temperature of water when the fat commences to rise in the tube. This temperature is recorded as the melting point.

The thermometer used in this test should be checked against a standard thermometer, calibrated and certified by the National Physics Laboratory, Teddington, England.

Note 2.—The Baudouin test shall be carried out as follows :—

Place in a test-tube 5 cc. of the sample (20 parts of vegetable oil products and 80 parts of refined groundnut oil) and 6 cc. of hydrochloric acid (specific gravity 1.19) and add to it 8 drops of 2 per cent solution in alcohol of freshly distilled furfural; shake vigorously for 2 minutes and allow to stand. The acid layer becomes distinctly red. Quickly filter the acid layer through a wet filter paper and examine the filtrate against a Lovibond scale in a 1 cm. cell or against a red colour comparator.

If the vegetable oil products on being shaken with hydrochloric acid alone, conveys a redness to the hydrochloric acid owing to the presence of certain artificial colouring agents, the procedure is as follows :—

Shake 10 cc. of the melted vegetable oil products in a separating funnel for half a minute with 10 cc. of hydrochloric acid, specific gravity 1.125. Draw off the red acid layer which collects at the bottom of the funnel and repeat the process until no further coloration takes place. During the treatment do not permit the temperature of the contents of the separating funnel to exceed that necessary to melt the fat. After the hydrochloric acid has been completely removed apply the Baudouin test as described above.

Non-hydrogenated groundnut oil.—The processed oil falling short of hydrogenation, and therefore not white in colour like ghee, is as good for cooking as the hydrogenated product and would be considerably cheaper. The manufacturers, however, do not approve of it. It is supposed to become rancid on keeping sooner than the untreated oil. As a matter of fact an untreated oil of a good quality is almost as good : the colour does not show in Indian dishes (excepting articles of diet made from flour and meant to look white), the odour is hardly perceptible and in spiced food a distinction is very difficult indeed. Its use should be encouraged. Studies on it have been undertaken (Ramamurti and Banerjee, 1948; abstract in this issue, p. 521).

Mineral oils used in cooking.—They have been used as adulterants and have even been recommended for slimming as they are not metabolized in the body. Their use, however, is not free from danger. Although liquid paraffin, heated and unheated, given to rats has not done any demonstrable harm, it is absorbed when dispersed in an emulsion in particles less than 0.5 μ in diameter. Continued ingestion may result in deposition of the oil in the intestinal wall, mesenteric glands and liver. Deposits in these localities have been found at necropsies on subjects who had taken liquid paraffin for years and died from various diseases (Editorial, 1948;

abstracted in the *Indian Medical Gazette*, October 1949, vol. 84, p. 474, Current Topics). Such deposits are obviously undesirable.

Edible fats and oils from chemicals.—A suggestion has been made that edible fats and oils can be prepared from CO (Hugh Sinclair, quoted by Chaudhuri, 1949). This perhaps will synchronize with tablets for food. The store, kitchen, pantry and dining room will then be accommodated in a small cupboard in the hall next to the First Aid cupboard in well-appointed residences.

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Medical News

FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

The following students are declared to have passed the L.T.M. Examination held on the 8th October, 1949, and subsequent days :—

Passed

(Arranged in alphabetical order)

- Dr. Sunil Kumar Acharyya, L.M.F. (Bengal), Assistant Medical Officer, Sonabheel Tea Estate.
 Dr. Krishnadas Bagchi, L.M.F. (Bengal), private practitioner.
 Dr. Birendra Nath Bhattacharjee, L.M.F. (Bengal), private practitioner.
 Dr. Anil Krishna Das, L.M.F. (Bengal), private practitioner.
 Dr. Kunja Lal Debnath, L.M.F. (Bengal), private practitioner.
 Dr. Panchu Gopal Ghosh, L.M.F. (Bengal), private practitioner.
 Dr. Nityananda Kundadas, L.M.F. (Bengal), private practitioner.
 Dr. Ranjit Kumar Mitra, L.M.F. (Bengal), private practitioner.
 Dr. Dhawaja Dhari Mukherjee, L.M.F. (Bengal), private practitioner.
 Dr. Ambarish Mukhopadhyaya, L.M.F. (Bengal), private practitioner.
 Dr. Karuna Kanta Roy, L.M.F. (Bengal), private practitioner.
 Dr. Adhir Kumar Samanta, L.M.F. (Bengal), private practitioner.
 Dr. Nripendra Chandra Sen, L.M.F. (Bengal), private practitioner.
 Dr. Sunil Kumar Sen, L.M.F. (Bengal), private practitioner.

- Dr. Chandrakant M. Shah, L.C.R.S. (Bombay), private practitioner.
 Dr. Suraj Narayan Sharma, L.M.P. (C. P.), Assistant Medical Officer, Beawar.
 Dr. Harbans Singh, L.M.F. (Bengal), private practitioner.
 Dr. Jagjeet Singh, L.S.M.F. (E. Punjab), private practitioner.
 Dr. Basant Kumar Soni, L.M.P. (C. P.), Pathologist, Victoria Hospital, Jubbulpore.
 Dr. Hiro Tuljaram Thadhani, L.C.P. & S. (Bombay), private practitioner.
 Dr. Vinay Chandra Upadhyaya, L.C.P. & S. (Bombay), private practitioner.

AMENDMENTS TO DRUG RULES, 1918

No. F.1-5/47-D., Government of India, Ministry of Health, New Delhi, the 25th November, 1949

NOTIFICATION

In exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendment shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said sections, namely :—

In the said rules, for Rule 107, the following rule shall be substituted, namely :—

'107. Name of substance.—If any substance specified in Schedule C is advertised or sold as a proprietary medicine or is contained in a medicine so advertised or sold, the proper name of the substance shall appear on the label in the manner prescribed in this part.

Explanation :—For the purpose of this rule, the expression "proper name" means the proper name stated in Schedule F or if no such name is stated, the name descriptive of the true nature and origin of the substance.'

(Sd.) J. N. SAKSENA,
Under Secretary.

(To be published in Part I, Section I of the *Gazette of India*, dated the 12th November, 1949)

No. F.1-7/48-D., Government of India, Ministry of Health, New Delhi, the 10th November, 1949.

NOTIFICATION

In exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendment shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said sections, namely :—

In Schedule D to the said rules :—

- The existing entry 5 shall be renumbered as 4.
- After entry 4 as so renumbered the following entry shall be added, namely :—

Class of drugs	Extent and conditions of exemption
----------------	------------------------------------

- | | |
|--|--|
| '5. Substances included in Schedule C(1) required for manufacturing purposes which are not intended for medical use in the form in which they are imported or which may be notified in the official Gazette from time to time. | The provisions of Chapter III of the Act and Rules thereunder which require them to be covered by import licences, subject to the condition that the exemption will be confined to holders of licence in Form 28.' |
|--|--|

(Sd.) J. N. SAKSENA,
Under Secretary.

JOURNAL OF SCIENTIFIC AND INDUSTRIAL RESEARCH: VERMICULITE, ITS ORIGIN, OCCURRENCE AND USES

(From Note No. 390, dated 14th September, 1949, issued by the Press Information Bureau, Government of India)

VERMICULITE was until comparatively recently an obscure mineral, with little or no practical application in industry. Within the last decade, however, it has come to occupy a leading place among the industrially important minerals, and the production of vermiculite is on the increase. A search for the mineral is being vigorously pursued in all countries.

Last year, some deposits of vermiculite were reported, for the first time in India, in the Tumkur District of Mysore State. The mica-like mineral was found to possess the peculiar property of exfoliation—slowly opening out, when heated, into long worm-like threads. A concerted search for the past year in other parts of the State has revealed that the mineral exists in considerable quantities in several localities.

An article in the September issue of the *Journal of Scientific and Industrial Research* deals with the composition, mode of occurrence, origin and distinguishing characteristics of the mineral, localities where it occurs, production costs and its industrial uses and applications.

World resources of vermiculite, at present, appear to be limited. The earliest known occurrence was probably at Libby, Montana, U.S.A. This deposit has been described as a hill, a thousand feet high and a square mile in extent, wholly composed of vermiculite. Other well-known deposits are in the Palabora district of the Transvaal, where reserves are estimated at 10 lakh tons. Important Russian deposits occur near Bulduin, in the Ural mountains. These are stated to be considerable and of commercial quality.

Mysore Deposits

From the report of a recent geological survey, four important deposits are known to be located in Mysore State: (1) The Bagoshpura area: No single prominent band has been traced, but the area over which the bands are distributed is very large. (2) The Channarayana area: A highly crumpled schist band 30 feet wide has been traced to a distance of 200 feet. Prospecting pits to a depth of 20 feet have shown vermiculite right through this depth. (3) Chunchankatte area: Here the vermiculite band is about 3 feet wide and traceable to a distance of a thousand feet. (4) Nidavanda area: Occurrences are thin, but the area is extensive.

Uses of vermiculite are based upon its property of being extremely light and at the same time refractory, with low conductivity to heat and sound. Exfoliated vermiculite weighs only 6 to 8 lb. per cubic foot and is therefore extensively used in concrete work in place of sand. Vermiculite concrete weighs only 25 to 50 lb. per cubic foot, compared with ordinary concrete which weighs 130 to 150 lb. This makes for reduced columns and beam sections and lighter foundations. The property that vermiculite has of holding small pockets of air between non-conducting fibres or plates makes it a good insulator. It is, therefore, used as an aggregate in insulating plaster and concrete. Vermiculite concrete, on account of its light weight and insulating properties, is used in making panels for prefabricated houses and roof decks. An inch of vermiculite plaster is stated to give four times the fireproofing effect of ordinary plaster. It is reported that an insulating block of vermiculite bonded with 25 per cent of colloidal magnesium silicate withstands a temperature of 2,000°F. Vermiculite concrete bricks are used for lining furnaces to withstand temperatures up to 1,600°F. The lining of domestic stoves with vermiculite concrete is stated to lead to decreased fuel consumption.

Sound Insulation

Because of the continuous channels connected with small pores which expanded vermiculite provides, it is useful for sound insulation and is extensively employed in radio studios, theatres and libraries to improve acoustics and reduce noise.

A new building material, 'Pyrok', has been developed in Great Britain from vermiculite. It consists of vermiculite bonded by a mixture of lime and cement. It is a surfacing material which is waterproof and fire resistant and adheres strongly to any surface, including wood, steel, asbestos and cement, and is free from the usual cracks evident in plaster. It is finding application in the ship-building industry as a coating to the underside of steel decking.

Expanded vermiculite has a pleasing golden-yellow colour, like that of gold dust, and the powdered material is used in wall-paper decorations. Another use of vermiculite is as a lubricating agent. It does not abrade, and the powder has lubricating properties similar to graphite.

Screened and cleaned vermiculite is sold at \$8 to \$12 per short ton, and exfoliated vermiculite at \$75 per ton.

Jellies from Tamarind Seed

A second article in the *Journal* describes the use of a new material, 'Tamarind Seed Jello', in the form of a water extract in place of fruit pectins in the preparation of jams, jellies, marmalades and jelly-fruit. The material is cheap and is easily obtained from tamarind seeds.

Tamarind seed jello forms excellent sugar jellies, with or without acid, and compares favourably in strength and transparency with those obtained from fruit pectins. Since the jello is a colourless, odourless and tasteless product, its addition does not in any way affect the natural colour, flavour and taste of fruit juices from which jellies are prepared.

The process of obtaining the jello is described in detail, and can be adopted on a cottage industry scale, as no special equipment is needed.

Other articles of interest in the *Journal* are: Two research papers relating to the germicidal properties of essential oils (lemon grass oil has been found to be the most effective); a paper dealing with the drying oil obtained from the seeds of 'snake gourd', *Trichosanthes amna* (the oil dries into a non-tacky film in about half an hour in the presence of cobalt linoleate dryer); an article on the properties of some Indian bricks made out of clays from different parts of the country.

AUSTRALIA IS A WORLD LEADER IN RESEARCH WITH RADIO-ACTIVE ISOTOPES

By LEN BARKER

(Reproduced from Release No. P/1267 issued by the Public Relations Officer, Australian High Commissioner's Office, New Delhi)

In the two years since radio-active isotopes have been available from the Oak Ridge (Tennessee) plant of the United States Atomic Energy Commission, Australia has become a leading consumer of these tracer elements. Up until the middle of 1948, research organizations 'down under' had absorbed more isotopes than any other country—despite the difficulties of distance which limited the quantity available.

Positive results have already been achieved and significant contributions to world knowledge in five or six branches of fundamental and applied research may be expected. Majority of the investigations are being carried out by Federal and State Government organizations, like the Commonwealth Scientific and Industrial Research Organization and the Victorian State Government's Department of Agriculture. Research completed

or under way covers fields in metallurgy, medicine, animal nutrition and agriculture.

Sheep parasite

Perhaps the most important to Australia—as the world's largest sheep producer—has been investigations at the C.S.I.R.O.'s McMaster Animal Health Laboratory of Sydney, into parasitical worms that infest the intestines of sheep and wreak havoc in flocks inflicted with it. Standard poison used to kill the worms is phenothiazine, but until the development of radio-active isotopes the exact dosage and best method of administering the poison were almost impossible to determine. Now, by introducing a radio-active isotope of the element sulphur into the poison, research workers have been able to find just how the parasites absorb it and in what quantities.

From this knowledge it is expected that research workers will be able to set standards for the administration of poison which will greatly improve on old methods.

'Tin Pest'

In the metallurgical field, original research has been made at the C.S.I.R.O.'s Division of Tribo-Physics into 'Tin Pest' and the rate of bearing-wear. 'Tin Pest' is a popular term which describes the tendency of tin to disintegrate at sub-normal temperatures. It was first observed during early Polar expeditions when, after battling through days of blizzards, explorers reached caches of food only to find that the cans had disintegrated through the cold.

Scientists assumed that the phenomenon was due to the extreme cold slowing down the movement of the molecules of the tin to the point where they no longer held together. Acting on this theory, they suggested that manufacturers of food cans make an alloy of tin and some other metal to stabilize the tin molecules. This proved successful, but from a fundamental scientific standpoint was a haphazard approach to the problem.

However, by attaching a tracer element (radio-active atom of tin) to molecules of tin, C.S.I.R.O. researchers have been able to study the movement of the molecules at extremely low temperatures. The data gained in this way have enabled them to decide the exact degree of impurity necessary to protect cans against Tin Pest.

By a similar technique of attaching tracer elements to metals, tribo physicists can measure to the last degree of accuracy, and in a few minutes, the amount of wear that takes place in a metal bearing, whereas in pre-radio-active isotope days, weeks of laborious tests gave them only a rough idea. One of the practical results of this is that it will now be possible to decide which is the best lubricant for a particular engine bearing.

Thyroid research

In medical research, radiologists working in conjunction with C.S.I.R.O. scientists have made effective contributions to knowledge of the behaviour of the thyroid gland. Radio-active iodine introduced into the gland has thrown further light on its activity and may provide more accurate methods of determining the dosage of radio-iodine necessary to cure or prevent thyroid disorders.

Control of the import and distribution of isotopes into Australia is the responsibility of the Federal Government's Commonwealth X-Ray and Radium Laboratory. Applications from research bodies for radio-active isotopes are made to a committee which investigates the claims. If they prove worthy, an order is placed with the United States Atomic Energy Commission for a parcel of isotopes of the element required. In turn the Commonwealth X-Ray and Radium Laboratory is responsible to the Commission to which it submits a six-monthly report of the use made of the isotopes. Recently, since England's Harwell Atomic Energy Station has been functioning, Australia has received, from this source also, supplies of various radio-active isotopes.



Im. (12)

ONE OF THE LARGEST HOSPITALS IN BRITAIN

The Royal Infirmary of Edinburgh, founded in 1729, is one of the largest general hospitals in Britain and one of the most up to date. This spotless operating theatre with the masked surgeon and nurses would have delighted Lister. During term time the gallery would be packed with students.

FIFTH INTERNATIONAL CONGRESS OF
SCIENTIFIC RESEARCH AND SOCIAL
CAMPAIGN AGAINST CANCER, PARIS

'THE Fifth International Cancer Research Congress will be held in Paris from the 15th to 22nd July, 1950, under the esteemed patronage of the President of the French Republic and the presidency of Prof. A. Lacassagne, Director of the "Institut du Radium", Paris.'

'The Congress will hold its sessions at the Sorbonne and the scientific meetings will commence on Monday, the 17th July, 1950.'

'At least fifty countries will be represented by eminent cancerologists of different nations.'

'All information regarding the Congress will be obtainable from Prof. V. Le Lorier, Secretary-General of the International Union Against Cancer, 6, Avenue Marceau, Paris (8e).'



Im. (7)

NEW HEARING AID

The 'Belelere' Radio Monopack, which is a high fidelity, single unit hearing aid, suitable for use in either slight or severe cases of deafness. It is easy to wear and is also extraordinarily economical for battery replacements. At the same time provision is made for receiving one radio programme without involving any extra control other than a change-over switch. The two controls are conveniently situated, one being the combined volume control and switch, and the other the infinitely variable tone control. No extra plug-in parts are necessary, and there is no need for an external aerial. Instead of switching your hearing aid off when you have no need to hear a conversation just switch over to radio and cultivate your powers of concentrating on listening.

Public Health Section

AIR-BORNE INFECTION

By H. S. ANDLEIGH, B.Sc., M.B., B.S., D.T.M. (Cal.),
D.Bact. (Lond.)

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THE prophylaxis of air-borne disease is a formidable problem which has in the past seemed almost insuperable. While general sanitary and administrative measures have proved effective in putting a check on the food and water-borne infections, this end has not been achieved in the control of air-borne infections. In the case of these infections it is particularly difficult, under modern conditions of civilization, to devise any generally applicable and effective means of preventing transit of the parasite from host to host. Sneezing, coughing and even talking are responsible for the spread of air-borne infections. These include :—

- Tuberculosis.
- Pneumonia.
- Pertussis.
- Diphtheria.
- Meningococci infections.
- Streptococcus throat.
- Scarlet fever.
- German measles.
- Chicken pox.
- Mumps.
- Poliomyelitis.
- Small-pox.
- Encephalitis.
- Colds.
- Influenza.

THE MEDIUM OF INFECTION

Flügge (1899) failed to recover nasopharyngeal organisms on plates exposed more than a few feet away from an infected patient, and concluded that infection was conveyed only by droplets coughed out or sneezed. As such, air-borne infection seemed almost eliminated. Cornet (1889) on the other hand dealing with the tubercle bacilli found that the chief source of infection was the dust arising from dried sputum. The mode of spread of common infections, however, suggested a mode of infection different from Flügge's finding and in 1931, Wells started his famous studies in air sanitation at Harvard. Wells (1934) found that the falling velocity of a small droplet is proportional to the square of its diameter, hence the smaller the diameter of the droplet the longer the time that it takes in settling down to the ground.

Wells also found that as these droplets fall, they evaporate and the rate of evaporation was inversely proportional to the square of the diameter, i.e. the smaller the diameter of the

droplet the quicker will it evaporate. The larger particles will therefore fall down quickly but as the water will remain in them for some time, they will retain droplet form, hence the term 'droplet-infection'. It has been found that droplets 100 microns or more in diameter behave like this. Droplets smaller than 100 microns in diameter behave differently, they remain suspended in the air for much longer periods, but since they soon lose their water by evaporation, they will quickly cease to be droplets and will become what Wells refers to as 'droplet-nuclei'. Several experiments have shown that dust particles of the size of 10 microns to 100 microns in diameter floating in the air are a potent source of infection. It is now generally accepted that the term 'droplet-infection' be applied to infection caused by droplets larger than 100 microns in diameter and 'air-borne' infection when the diameter of the particle is less than 100 microns. Thus we see that in considering infection by bacteria or viruses through the medium of air, we have to take three things into consideration. (1) The droplets, (2) the droplet-nuclei and (3) the dust. The characters of each are given in the table.

SURVIVAL OF THE INFECTIVE AGENTS

Various experiments have shown that the infective agents, i.e. bacteria and viruses, survive in air for a fairly long time. Garrod (1944) was able to culture from hospital dust colonies of streptococci of a type which had been responsible for a ward epidemic 195 days earlier. Downie (1947) showed that small-pox virus could be isolated from crusts left exposed in a room, up to 2 years. Also animal experiments have shown that the droplet-nuclei can be carried in air, and penetrate through the depths of lung.

Measures of control.—It is thus established that the air itself acts as a vehicle for the transmission of the infective agents which can also survive in this medium for long periods. The measures of control are therefore concentrated on two things: (1) To prevent the infection of the air as far as possible. (2) To make the air free from the infection as far as possible, in case it gets infected. As the measures differ in the three types of infection, they will be dealt with individually.

DUST-BORNE INFECTION

As Andrews (1940) points out, no method for control of air-borne infection is as satisfactory as proper spacing of individuals combined with adequate ventilation. These enormously reduce the risk of infection, whether from the droplet nuclei or dust. Every attempt should be made

TABLE

	Dust	Droplets	Droplet-nuclei
Sources of material ..	Solid matter, fabrics, etc.	Fluids from nose and throat	Solid residue of evaporated drop.
Production ..	Attrition (friction)	Atomization of fluids	Evaporation of droplets.
Mode of suspension ..	Air-wafted	Projected into air by sneezing, etc.	Caught in air by evaporation.
Particle diameter ..	10-100 μ	Larger than 100 μ	2-10 μ
Settling velocity ..	1 foot per second to 1 foot per minute.	1 foot or more than 1 foot per second.	Less than 1 foot per minute.
Time of suspension in air.	They remain in the air for a variable time and wafted about by air.	They fall to the ground in a few seconds, <i>i.e.</i> less than 30 seconds.	Also in air for a variable time.
Flight range ..	Hovers in clouds	Immediate in space	Dispersed throughout indoor atmosphere.
Concentration ..	Locally high	Immediately intense	Diffuse and dilute.
Organisms carried ..	Mostly saprophytic	Parasitic and pathogenic	Parasitic and pathogenic.
Bacteria/particle ..	Clumps	Indeterminate	Seldom more than one.
Inhalation ..	Trapped in nose and throat	Indeterminate	Penetrate to lung.
Mode of infection ..	Endemic infection of nose and throat.	Contact infection	Epidemic contagion.
Vulnerability ..	Resistant to various agents known at the moment.	Vulnerable according to their size.	Vulnerable to chemicals and physical agents.

for spacing out and all other measures of control considered in addition to these and not as their substitutes. Dust-borne infection can be best controlled by dust suppressive measures. The organism-laden dust sediments quickly to the ground and then, if it is not allowed to spread up again during sweeping, etc., the danger from it may be very much minimized. This can be best achieved by the application of oils to wooden floors and linoleum floors. The oil used is spindle oil. It has been found that if the floor was treated with spindle oil, the dust particles will become sticky and mutually adherent, so that they could be swept away without being dispersed again into the air. The oil can be applied to the wooden and linoleum floors, but not to the rubber, cement or concrete floors. One application would last for about 8 weeks. One gallon of oil will be sufficient for 1,800 square feet. For lino the best thing to do is to mop it daily with oiled sawdust.

In hospital, patients' clothes and beddings, covers and blankets, etc., should also be oiled so that no fibre particles are wafted about during bed-making. The laundry people have developed a technique so that the clothes finally do not feel much different from the normal clothes.

DROPLET-BORNE INFECTION

The only real way of preventing droplet-infection is the education of the masses in the

basic sanitary and hygienic principles, including the proper use of the handkerchief and the face-mask. To be of any real use, the face-mask must contain a piece of cellophane. As mentioned above, spacing out will particularly be very helpful.

INFECTION CARRIED BY DROPLET-NUCLEI

Measures to control the aerial infection can be grouped under two heads: (1) Disinfectant sprays and vapours and (2) ultra-violet rays.

Disinfectant sprays and vapours.—The substances used for this purpose are, sodium hypochlorite, resorcinol, hexyl-resorcinol, droplene-glycol, methylene-glycol and incense (smoke), etc. These methods are not very refined and pleasant, they are tedious, and they are not readily available any and every moment. The best method up till now is the ultra-violet irradiation.

Ultra-violet irradiation.—It was discovered by Downes and Blunt in 1877 that ultra-violet rays destroyed bacteria. It is now known that the bactericidal action is exercised particularly by the short rays of the ultra-violet spectrum, the maximum effect being associated with wave length 2,600 to 2,500 A.U. For purpose of destroying bacteria the most effective source of ultra-violet rays is found to be a Geissler low pressure mercury discharge tube of quartz. This generates 95 per cent ultra-violet rays (*i.e.* 85

per cent of its total output) in a band at 2,536 A.U. The most effective method of applying ultra-violet irradiations is to operate the bactericidal tubes within the fluid itself, that is the air of the room. The method can be adopted in two ways : (1) Indirect or upper air irradiation for normally inhabited rooms, and (2) direct irradiation in special cases (*i.e.* unoccupied process rooms or where masks and eye-shields are worn). This applied by whichever method ultra-violet rays will disinfect air many times faster than can be effected by any system of natural or mechanical ventilation and without any sophistication of the air by chemicals. In designing an installation two factors are important for consideration :—

1. The degree of contamination of the air at the site.

2. Conditions of human occupancy.

In India as we have bright sunshine for most part of the year, the outdoor air seldom contains harmful bacteria and never harbours them long. Indoors, however, they are present in any inhabited room, exhaled by the occupants or shed from their clothes, etc. Drs. Bourdillon and Colebrook (1946) in England found the following figures for total organisms per cubic foot of air in different environments :—

1. Engineering shop (high roof, oily floor).	..	4-20
2. Busy offices	15-60
3. Crowded canteens	50-250
4. Hospital wards (normal activity).	..	10-100
5. Hospital wards (during bed-making).	..	Up to 2,000

Taking the same figures, if not more, for India, we have to say that there is a heavy degree of pollution of air in the hospital wards, cinema houses, crowded canteens and business offices. In the hospital wards the condition, *i.e.* the special risk of cross-infection and constant occupation by sources of infection, indicates all possible precaution against air-borne bacteria. It will, therefore, be advisable to instal ultra-violet lamps in the hospitals for purposes of air disinfection. Furthermore, public places such as the cinema halls should also be disinfected with ultra-violet irradiation. While the above methods are very helpful in reducing considerably the incidence of air-borne infections, some gaps are still left behind which are difficult to fill. In the prevention of enteric infections, reliable measures are available for effecting a constant supply of pure and disinfected water, and the water-borne infections have completely been checked. In the case of air-borne infections, even if we protect one in the wards or the cinema houses, we cannot do so constantly during all his movements. Another difficulty is to ensure the continuous absence of pathogenic organisms from the air during the 24 hours each day. Therefore an intensive and prolonged

education of the general public in the basic principles of hygiene and sanitation is of utmost importance.

For the present, therefore, along with the extensive education programme, it will probably be wise to confine our attention to the prophylaxis of air-borne infections in such situations as operation theatres, hospital wards, out-patients' departments and the cinema houses.

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The Indian Medical Gazette Fifty Years Ago

LONDON LETTER

Scarlatina in India

(From the *Indian Medical Gazette*, 1899, Vol. 34, p. 414)

By a happy coincidence the question of the prevalence of Scarlet Fever in India and other tropical countries has been simultaneously raised in the *Journal of Tropical Medicine* and in your own pages. The subject has been from time to time discussed in the *Indian Medical Gazette* since the year 1870. It has been made quite certain that Scarlatina has been repeatedly imported into India by means of troop-ships, and that in this manner small outbreaks have arisen in military stations and among civil communities, both on hills and plains. It has also been conclusively proved that these epidemics are very limited both in space and time.

It has been inferred that India and other tropical countries possess an immunity as regards this disease, that is to say, that the microbe which presumably causes it belonging as it seems to do the class of obligatory parasites, does not find in tropical conditions favouring circumstances for life and propagation. Once admitted into the individual, it appears to give rise to the same pathological phenomena as in temperate countries. It must therefore be during the interval of transit from the diseased to the healthy subject that it encounters an environment inimical to either

existence or virulence or both. The exact truth of its natural history, somatic and extra-somatic, remains to be worked out, but the facts already ascertained justify these provisional conclusions. The curious and really important fact, which the papers to which I have referred place in evidence, is that an eruptive, febrile disease, presenting close if not complete clinical resemblance to Scarlatina, arises sometimes in India *de novo*, and that occasionally such cases occur in groups and seem to result from communication. I have myself seen such cases singly and in groups in Calcutta and at Darjeeling, and they have been met with by others, as the literature on the subject shows. In these instances the question of importation has been held in view; but the circumstances of their occurrence were, in most cases, such as to render this mode of origin extremely unlikely; and it seems absolutely true that, as in imported cases, so in these autogenous cases the power of infection is exceedingly weak, the incidence very limited, and the duration of outbreak short. The aspect which has been displayed is that of a disease epidemic under favouring condition, which is capable of implantation or even origin *de novo* but incapable of propagation. The matter is therefore one of profound interest both pathologically and epidemiologically, and it is to be hoped that, as opportunity offers, by general, clinical and bacteriological methods, the points above mooted will be eventually cleared up both as regards India and the tropics generally.

The Physical Requirements of the Public Services

An important discussion took place in the section of medicine at the meeting of the British Medical Association at Portsmouth on the medical tests for admission to the Public Services. The time and place were well suited for ventilating questions which concern the efficiency of the services, the anxieties of parents and guardians and the interests of so many youths. The particular subjects of attention were—(1) propriety of existing standards of physical fitness; (2) the methods by which examinations for physical fitness are at present conducted; (3) the uniformity and fairness of such examinations; and (4) the time when they ought to be held whether before or after the literary examination. On these points a considerable variety of opinions were offered, and the only subject on which the section appeared to be unanimous was the stage of the competitive examination at which the testing for physical fitness should be conducted. In effect it was decided that the elimination of the physically unqualified ought to take place before the candidates are subjected to a trial of their intellectual capacity. The reason for this, which seemed to weigh with the section, was that it was cruel to subject youths to the pains of a

tiresome literary examination and the disappointment of subsequent rejection, on account of physical incapacity, after they had passed it and perhaps passed it creditably. There is some sense in this view, but it does not wholly express or meet the hardships of the case, for rejection immediately before examination, does not take into account the wasted time, labour and expense of preparation, or the disappointment and demoralizing effect of failure after years of study and expectation, both with a special object. The real truth is that physical fitness should be as far as possible tested and ascertained before a boy commences to study for any particular service in which this is laid down as a necessary qualification. The State cannot be expected to perform a service of this kind for the multitude of youths scattered throughout the Empire who may contemplate preparing themselves for State Employment, nor could it be reasonably held to abide by the results of such early examination, so that a further testing immediately before or after the examination would still be necessary. It is the civil practitioner or the retired army or navy surgeon who should be entrusted with this duty; and by a little study of the regulations issued by public departments and boards of examination, it could be fulfilled with sufficient success to indicate whether a boy should undertake the task of preparative study or not just as the report of the headmaster of his school decides, whether he possesses the necessary intellectual capacity and industry for same end.

Some public departments—the Admiralty for example—pointedly recommended these preliminary medical examinations and there can be no doubt that they ought invariably to be made; and if this became the practice, specialists would be forthcoming, who would qualify themselves to give sound advice. In civil life, physical fitness, if at all enquired into, is considered after selection for employment; but everything depends on the kind of employment and the degree of physical capacity which it demands. In the Army and Navy, physical capacity must necessarily hold a high place, and the question has frequently arisen, whether the element of competition should not apply to this as well as to intellectual endowments by assigning marks for physique, endurance, robustness, agility, and so forth. This has hitherto been found impracticable, and standards have been laid down for the guidance of boards, which cannot be pronounced unreasonable nor unfair; nor can boards be accused of applying these with undue severity or eccentricity.

The Cultivation of the Quartan Parasite in the Mosquito

Major Ross has telegraphed from the West Coast of Africa that he has succeeded in cultivating the parasites of quartan fever in anophelids, the genus of mosquito in which the tertian and

summer-autumn parasites have already been grown. This is an important announcement, and in response to Major Ross's appeal for additional workers, Mr. R. Fielding Ould, M.A., M.B. (Oxon.), has been deputed to join him at Sierra Leone, and assist him in carrying on his investigations.

KENNETH McLEOD.

9th September, 1899.

Current Topics, Etc.

The Extirpation of Tuberculosis

(From the *Medical Officer*, Vol. 81, 5th March, 1949, p. 102)

A RECENT address by Dr. C. O. Stallybrass revives an old question: Can we stamp out tuberculosis? The fatalistic attitude to consumption of the mid-Victorian era gave place to optimism after Koch's discovery and for 60 years we have alternated between hopes and fears, with new promises and disappointments. A disease in the ætiology of which there is an essential factor, separable from and not produced by physiological economy and which is destructible, is capable of extermination; but whether the difficulties of doing this are in practice surmountable is another question.

Tuberculosis has existed from time immemorial and at present attacks all vertebrates, though in very variable degree. Hippocrates was familiar with phthisis in man, but we know little of its history between his time and the eighteenth century. There seems to be no doubt that the industrial revolution led to an enormous increase in tuberculosis and about 100 years ago, in the era of great fiction, it had become a major factor in English life. From that time the disease has steadily declined. In 1847, the mortality from phthisis in England was 3,189 per million and we may guess that if other forms of tuberculosis are included it was not short of 4,000. To-day the mortality is round about 500, or roughly one-eighth of what it had been. Apart from a few temporary jumps, the graph of tuberculosis mortality has been a steady slant downwards and though the decline has decelerated, it still continues. This suggests that the disease is dying out naturally; but there are many reasons to think that this is not the case. In the last 100, and specially in the last 30, years man has been actively engaged in the suppression of tuberculosis and from time to time has introduced new measures of great promise. None of these measures produced any obvious effect on the general graph of mortality. This does not mean that they had no influence; it can be shown conclusively that they have considerable influence.

Stallybrass says that the greatest factor in causing the fall of tuberculosis in the nineteenth century was the rise in the real value of wages. If this was so, and we do not doubt it, the fall would naturally be slow and progressive, for though actual wages fluctuate widely and suddenly their real value does not. The abolition of poverty greatly reduces the toll of tuberculosis, but it would not cause the extermination of the disease. To do this one of four things must happen: man must develop immunity to *Mycobacterium*, or *Mycobacterium* must lose its pathogenic power, or be exterminated, or an absolute barrier must be erected between the parasite and its hosts. Only the second or third would result in the complete extinction of the

disease. There seems no hope that *Mycobacterium* will lose its pathogenic property, but extermination, at all events in a limited field, is not possible; e.g. herds of tuberculosis-free cattle. These, however, can be maintained only by constant supervision and by means not applicable to man.

Our main hope lies in immunity, if this is used in widest sense of that word, for in its limited technical sense there is no evidence that it exists. Yet some animals have developed a natural immunity. This is most remarkable in sheep, for the nearly related cattle are highly susceptible. Races of men, or rather communities, which have been long exposed to tuberculosis, are more resistant than those that are virgin. Increased resistance as a biological evolutionary process can hardly have made much progress in the past 100 years, so we can dismiss it as the explanation of the fall in tuberculosis between 1847 and 1947. We believe the main reason for this fall is a combination which has produced diminution in the size of dosage, especially of the first shot. Some animals, guinea-pigs for instance, have no resistance to *Mycobacterium* even in a minute dosage: Stallybrass says one solitary bacillus will cause fatal disease. Man is far less susceptible, for the process of tubercularization shows clearly that man can resist minimal doses and probably the resistance is increased by repetition even though true immunity never results from it. This brings up the question of the value of inoculation, either by B.C.G. or the vole strain. Here the dosage is large, but of strains which are not pathogenic to man, or so slightly so that the risk can be ignored. The theoretical grounds for expecting much success from vaccination seem to us to be slight, but where it has been adopted on a large scale, its validity is firmly held and it may prove to be the weapon which will complete the conquest of tuberculosis, on condition that too much reliance is not placed on it, leading to neglect of other means of combating the disease. B.C.G. is on the same principle as Jennerian vaccination, but there is little in common between tuberculosis and smallpox in which reaction results in a strong immunity.

The Histology of the Endometrium in Functional Uterine Hæmorrhage: Analysis of 1,000 Cases and Review of the Literature

By A. M. SUTHERLAND

(Abstracted from the *Glasgow Medical Journal*, Vol. 30, January 1949, p. 1)

AN analysis was made of the histological findings in 1,000 cases of abnormal uterine bleeding in the absence of gross pelvic pathology, all patients with bleeding after the menopause being excluded.

In 139 instances organic pathological lesions of the endometrium were found. Chronic endometritis occurred in 110 cases, uterine polypi in 11 cases, tuberculosis in 10 cases and malignant disease in 8 cases. These figures demonstrate the necessity for routine diagnostic curettage in all cases of presumed functional bleeding, irrespective of age.

In the remaining 861 cases no organic pathological conditions of the endometrium were found. Endometrial hyperplasia occurred 265 times, endometrial atrophy 10 times, irregular shedding of the endometrium 13 times and irregular ripening of the endometrium 26 times. In the remaining 547 specimens the endometrium appeared normal.

In 9 of the organic group and 48 of the functional group the endometrium was examined on more than one occasion. The altered histology in many of these repeat specimens is discussed.

Attempts to correlate the histological appearances with the type of bleeding and with the findings on pelvic examination failed to demonstrate any relationship in either instance.

It was finally apparent that almost any type of abnormal uterine bleeding can occur from any type of endometrium and that any attempt at diagnosis of functional bleeding without histological examination of the endometrium is quite unjustifiable.

Indications for the Removal of Teeth

By R. S. TAYLOR

(Abstracted from the *Medical Press*, Vol. 221, 19th January, 1949, p. 57)

To summarize this paper, one can say that teeth are removed in the adult for the purpose of eliminating sepsis, to make it easier to restore function, and in a certain number of cases to improve appearance by the provision of a more pleasing artificial substitute.

While the removal of teeth is probably the most efficient method of removing sepsis, the treatment of the supporting bone must be considered. Mere removal of a tooth even though such removal is complete, may not always eliminate all sepsis from the mouth. The part played by retained roots as sources of sepsis must not be forgotten. In the case of a young patient teeth may be removed to treat sepsis and in a certain number of cases with the purpose of relieving overcrowding so as to improve the function of the dental arch and to give a better appearance. The removal of deciduous teeth should be avoided, and this can only be done by frequent inspection and careful attention during infancy.

It is hardly necessary to warn the physician not to consider the removal of teeth as some magic cure-all.

Sudden Death of Babies

(From the *Medical Journal of Australia*, Vol. 1, 26th February, 1949, p. 275)

Few things are more shocking to the general public, and especially to parents, than the sudden death of an apparently healthy baby. Particularly disturbing to conscientious parents is the type of death recently reported, and occurring from time to time, in which the child has been found face downwards in the cot or bassinet and the coroner has brought in a verdict of death by asphyxiation, the child apparently having smothered itself accidentally with its own pillow. Another type of death appears to be due to the inhalation of food particles particularly when vomiting is associated with crying. Last year an anonymous article appeared in a well-known American magazine apparently written by the father of a boy, aged ten months, who was found dead in his crib. The story was that the baby had an area of irritation on the back of his head and the doctor advised the mother to put the baby face downward during his nap. This the mother did. The baby was heard to cry and vomited a part of his previous meal; when the parents reached the bed he was dead. The father felt that the death was due to the fact that the child was placed in the prone position on the doctor's advice and was apparently very critical of the medical profession for giving such advice. The question was referred by a doctor to the 'queries' column of the *Journal of the American Medical Association* for an opinion. In the reply it was stated that the evidence was insufficient to prove that the prone position of itself was the cause of sudden death. Anyone who has observed the sleeping

habits of babies, as in a hospital ward, will know that many sleep in the prone position by choice, with no apparent ill effects. The reply to the query stresses, however, the importance of a firm mattress completely filling the cot, so that the child may not bury his face in it or become wedged between it and the side of the cot; pillows are proscribed completely. In an analysis of deaths of infants recorded at the Leeds coroner's court, C. J. Polson and D. E. Price state that soft feather pillows were the factor responsible in two deaths and probably also responsible in another two. It is not quite clear what they mean, but as their discussion refers primarily to deaths associated with vomiting, it is doubtful that they imply the occurrence of suffocation by the pillows alone. They stress the importance of careful preparation of artificial milk foods to ensure that lumps are avoided and refer unfavourably to the practice of enlarging the opening of a teat so that these lumps are sucked through. The American discussion also refers to asphyxia due to the aspiration of food particles, including milk curds and mucus. It seems logical enough that an infant face-down on a soft pillow or mattress will more readily aspirate vomitus than if it has free means of escape, and the wisdom of the firm mattress and pillow (if any) is apparent. Australian authorities recommend to mothers the use of a fibre mattress with a light chaff mattress on top and a small chaff pillow, and this would seem to meet the situation. The question of death apart from vomiting remains vexed. The reply in the American journal lists, among reported or conjectured causes of sudden death, accidental strangulation with bands of clothing, blankets and restraining garments, acute broncho-pneumonia, spontaneous hæmorrhages into the lungs of peritoneal cavity, apoplexy of adrenal glands, hyperacute attacks of fever as in meningococcus infections, anaphylactic shock, laryngospasm of tetany, and hyperglycæmia due to adrenal insufficiency, and accepts the occurrence of simple self-asphyxiation with a pillow while rejecting the once popular 'thymic death'. The problem is by no means fully resolved; there is room for careful investigation and need for the development of prophylactic measures.

The Streptomycin-Sulphadiazine Treatment of Undulant Fever

By E. F. SCOWEN

and

L. P. GARROD

(Abstracted from the *British Medical Journal*, ii, 25th December, 1948, p. 1099)

THE results of chemotherapy in undulant fever have hitherto been disappointing. *Brucella abortus* is sensitive to sulphonamides, but a full course of treatment with these drugs, though often of temporary benefit, does not usually eradicate the infection: possibly sulphadiazine together with blood transfusions, as recently advocated by Holmes and Hughes, may give better results. Penicillin is useless owing to the insensitivity of the organism. On the other hand, *Br. abortus* is sensitive to streptomycin, its growth being inhibited by from 0.5 to 3.75 µg. per ml., a finding well within limits compatible with successful treatment.

We have had the opportunity of testing this treatment in two severe cases of undulant fever—one at an early and one in a later stage. The regime decided on was 2 g. of sulphadiazine four-hourly (i.e. 12 g. daily) by mouth, and 1 g. of streptomycin eight-hourly (3 g. daily) by intramuscular injection, continued for fourteen days. In both cases the treatment seems to have been completely successful.

Of these two cases, one was of several months' duration and the other was recent. Both responded to combined treatment with streptomycin and sulphadiazine, the former with a fall in temperature to normal within three days, the second somewhat more gradually, the temperature reaching normal only at the end of the course. They have now been afebrile for six and two months respectively. These observations confirm American reports of the efficacy of this treatment.

Creeping Eruption and Intestinal Strongyloidiasis

(Abstracted from the *British Medical Journal*, i, 5th March, 1919, p. 396)

CREeping eruption resulting from the exposure of the unprotected skin of man to mature filariform larvae of canine, feline and human hookworms in moist shaded soil contaminated by the infected faeces of dogs, cats or man is well recognized. In the vast majority of cases, however, the skin lesions have mainly affected the hands and feet; in one case the migrating larvae was observed wandering over the hand for as long as twenty-four hours.

In January 1946, during a routine clinical examination of a patient admitted to the tropical diseases unit of Queen Mary's Hospital, Roehampton, it was noted that he had a tortuous linear urticarial weal affecting his buttock, starting near the anus and extending upwards towards the iliac crest. It was intensely itchy and progressed at a rate which was later found to vary from two to four inches (5-10 cm. an hour). This rate of progress is much in excess of that of the hitherto described forms of creeping eruption, which vary from a fraction of an inch to several inches in twenty-four hours. The patient was an ex-prisoner-of-war from the Far East and had worked on the Burma-Siam railway. Investigation showed him to be suffering from both ankylostomiasis and strongyloidiasis, but despite the successful treatment of ankylostomiasis the creeping eruption persisted, as also did the strongyloidiasis.

It was subsequently noted without exception in a series of several hundred cases that this type of creeping eruption—i.e. a tortuous or serpiginous linear urticarial weal—occurred only in ex-prisoners-of-war from the Far East, and that they had been held in captivity in grossly insanitary conditions in Burma and Siam, with one case from Java. Their blood picture showed an eosinophilia varying from 10 to 25 per cent, with a total white cell count often within normal limits giving absolute eosinophil counts of 700 to 2,000 per c.mm.

Apart from less than 2 per cent of all cases of creeping eruption in which no helminth ova or larvae could be found on repeated microscopy, including after purgation and by concentration methods, all the cases have been associated with the finding of larvae of *S. stercoralis* in the faeces. In cases in which there was multiple helminth infestation, the creeping eruption has persisted to date despite the eradication of all helminths other than *S. stercoralis*.

The creeping eruption begins in most cases in close proximity to the anus; it may extend downwards, affecting the upper third of the thigh, but has never been observed below this. It also affects the buttocks and the posterior and lateral aspects of the body as far upwards as the shoulders, but has not extended into the arms beyond the axillary folds. Anteriorly it occurs over the lower half of the abdomen, not affecting the external genitalia, and in some few cases the anterior surface of the chest has shown the characteristic lesions. It causes considerable itching and irritation.

Definite proof of the causation of the creeping eruption by wandering larvae of *S. stercoralis* is still

lacking. Gentian violet, hexyl-resorcinol, antimonials such as sodium stibogluconate, lithium antimony thiomalate, and 'hetrazan' have all proved uniformly successful.

Fortunately the skin irritation has been found to be amenable to symptomatic treatment with the antihistamine group of drugs.

Urea-Sulphonamide Therapy

(From the *Lancet*, i, 15th January, 1949, p. 112)

It was in the 1914-18 war that urea was first used for the treatment of infected war wounds. Then it seems to have fallen into disuse until 1937, when Holder and MacKay reported the effective treatment of infected or potentially infected wounds with sulphonamide-urea mixtures containing about 10 per cent of urea. These workers claimed that urea was non-irritating to tissues and exerted its beneficial action by dissolving the pus and necrotic debris of wounds, which contains sulphonamide inhibitors. They also showed that urea increases the solubility of sulphanilamide and sulphadiazine in tissue fluids and that *in vitro* the bacteriostatic effect of sulphanilamide against *Bact. coli* is increased tenfold by the addition of 5 per cent urea. Tsuchiya and his co-workers extended these observations to other sulphonamides and showed *in vitro* that urea significantly increases their bacteriostatic effect even in the presence of known sulphonamide inhibitors such as *p*-aminobenzoic acid and methionine. Perhaps more important they demonstrated that strains of sulphathiazole-resistant staphylococci in a synthetic medium were susceptible to combinations of urea and sodium sulphathiazole.

The development of sulphonamide resistance has now become of considerable practical importance in therapeutics, and any agent which may overcome this resistance deserves careful study. The local use of urea with sulphonamides is now well established, but urea is likely to be of greater therapeutic value in the treatment of sulphonamide-resistant infections, particularly those not amenable to treatment with penicillin. Apart from increasing the bacteriostatic action of the sulphonamides, urea increases their solubility, so that large doses can be given without fear of crystalluria. La Londe and Gardner have treated five cases of meningitis with urea and sulphadiazine. The adult dose of urea was 30 g. four-hourly by mouth. One case was due to *Bact. faecalis alkaligenes*, which did not respond to penicillin and sulphadiazine alone, and in which streptomycin was not tolerated. Another was a case of meningitis due to *Friedländer's bacillus*, which developed while the patient was receiving prophylactic doses of penicillin. There were also two cases of meningitis due to *Bact. coli* and one probably due to *Staphylococcus albus*. There was good evidence that the urea-sulphonamide therapy was responsible for these patients' recovery, and since it is simple, safe and inexpensive, it merits trial in sulphonamide-resistant infections before resorting to streptomycin.

Substitutes for Plasma

(Abstracted from the *Lancet*, i, 22nd January, 1949, p. 151)

THERE are occasions in this country in peace-time when a substitute for plasma would be useful, and it would have great value abroad wherever plasma is unobtainable or is liable to deteriorate. Its possible importance in time of war is obvious.

Most of the substances proposed and tested have failed to meet one or more of the theoretical requirements of a plasma substitute set out by Dr. Bull and his colleagues in our present issue. Gum-acacia was

suspect before the late war. Of the many other substances investigated—pectin, gelatine, bovine albumin, bovine plasma and serum, isinglass, methyl cellulose polyvinyl pyrolidone, polyvinyl alcohol, ascitic fluid, and the glucose polymer dextran—all seem to have disadvantages, except perhaps the last, which is now receiving closer attention. Though its possibilities were considered in England early in the war, the credit for producing dextran in a form suitable for infusion belongs to the Swedish workers Grönwall and Ingelman, Bohmansson *et al.*, and Dr. Thorsér whose latest paper we publish this week. Dextran is now freely used in Sweden, where there is no nation-wide transfusion service, and, judging by published reports, experience has been uniformly favourable. Corroboration is now provided by the results of a laboratory and clinical trial of British-made dextran, by Dr. Bull and his colleagues, showing that it is a bland, non-toxic, non-antigenic fluid which, in cases of burns and in subjects suffering from 'shock' or hæmorrhage, appears to be as beneficial as plasma. It seems to fulfil the theoretical requirements with the single exception that its disappearance from the body is probably slow. Whether it is completely metabolized as glucose, or whether it is broken down to lower molecular weight and slowly excreted, remains to be seen. *Continued from p. 515* reported histological changes in temporary—after its use, but they do not clearly define the type of dextran they infuse; and introduction of dextran into animals in quantities larger than any likely to be given to human beings has caused no such changes. Dextran molecules smaller than 70,000 are excreted within a comparatively short time, and it is possible that, where renal function was already depressed, the added excretory load thus imposed might be dangerous. This possible drawback might well be overcome if dextran could be prepared, as Dr. Bull and his colleagues suggest, without the small molecular fraction.

One of the great merits of dextran is that it can probably be manufactured to conform closely to the ideal specification of an artificial substitute for plasma. We hope, therefore, that the more extensive trial proposed by the British workers will be carried out, so that the fate of the dextran in the body, and any remote harm it can do, may be fully revealed. Its keeping qualities under tropical and other climatic conditions also need investigation.

Acquired Resistance to Proguanil (Paludrine) in *Plasmodium vivax*

By D. R. SEATON
and

E. M. LOURIE

(Abstracted from the *Lancet*, *i*, 5th March, 1949, p. 394)

RESISTANCE to proguanil was produced in a strain of *Plasmodium vivax* by giving small doses of the drug to consecutive patients in a series in whom the strain was being maintained by blood-inoculation. The resistance was unaffected by passage through mosquitoes.

Though the resistance acquired was more than eighty times greater than normal, it was only within the last few weeks of the investigation that the strain became resistant to doses within the ordinary therapeutic range.

The fact that this degree of resistance did not arise at an earlier stage, though conditions were specially designed to favour its development and were continued for more than 20 months, indicates that the danger of producing a serious degree of resistance in a strain of *P. vivax* by the ordinary use of proguanil in clinical practice is very slight, if not negligible. This conclusion is reinforced, as regards the suppressive use of proguanil, by the recent finding that resistance in fowl

malaria cannot readily be produced by treating latent, as distinct from acute, infections.

Paludrine in Malaria : Dosage for Prevention and Treatment

(From the *Lancet*, *i*, 2nd April, 1949, p. 578)

THE following recommendations on the use of proguanil ('Paludrine') in prophylaxis and treatment of malaria, and, are issued by the Colonial Office Research Council on the advice of the Colonial Medical Research Committee. The recommendations are tentative and subject to review in the light of future experience and experiment.

PROPHYLACTIC USE

The dose recommended for suppression of malaria of all types, in endemic areas, is 100 mg. daily. For children the following dosage is advised: from birth to 5 years of age, 25 mg. daily; from 6 to 12 years of age, 50 mg. daily. When a daily dose is not practicable, one dose of 300 mg. should be taken on the same day each week; dosage of children should be in the above proportion. In the case of persons (other than indigenous inhabitants) who have been resident in an endemic area for some time, or who have been otherwise already exposed to malarial infection, a full therapeutic course [see 1 (a) below] should be taken before entering on the suppressive regimen of paludrine.

THERAPEUTIC USE

1. *Plasmodium falciparum* (malignant tertian) infections, mixed infections, undiagnosed type infections

(a) In the treatment of non-immunes, paludrine alone cannot always be relied upon to effect radical cure, and the clinical response with this drug unaided is also somewhat slow. It has been shown, however, that these disadvantages may be overcome by reinforcement with mepacrine on the first day of treatment. The following combined course is recommended for trial: 300 mg. paludrine twice daily for 10 days, reinforced on the first day of treatment with three doses of 300 mg. mepacrine, and followed by 100 mg. paludrine daily for six weeks. (Persons continuing to live in an endemic area should continue the suppressive regimen.)

(b) For treatment of the clinical attack in semi-immune subjects, such as labour forces and rural populations in endemic areas, a single dose of 300 mg. paludrine will usually suffice to produce clinical cure. Relapses can be treated similarly as and when they arise. Serious cases should be given emergent treatment (see below).

(c) For treatment of emergent conditions such as cerebral or algid malaria, and where for any other reason the patient is unable to take drugs by mouth, immediate intramuscular mepacrine or intravenous quinine therapy should be employed.

2. *P. vivax* (benign tertian) infections

(a) Where the object is radical cure, the course advised for adults is 100 mg. paludrine plus 10 mg. pamaquin base (or a corresponding dose of one of the other 8-amino-quinoline derivatives) three times daily for 10 days; the dose for children should be proportionate. Pamaquin should not be given unless the patient can be kept in bed under medical supervision throughout the course; this is particularly important with children. When the patient cannot be kept in bed, the alternative course recommended is 100 mg. paludrine three times daily for 10 days followed by a single dose of 300 mg. of paludrine on the same day each week for a year.

(b) The treatment of the clinical attack in semi-immunes is as for M.T. malaria.

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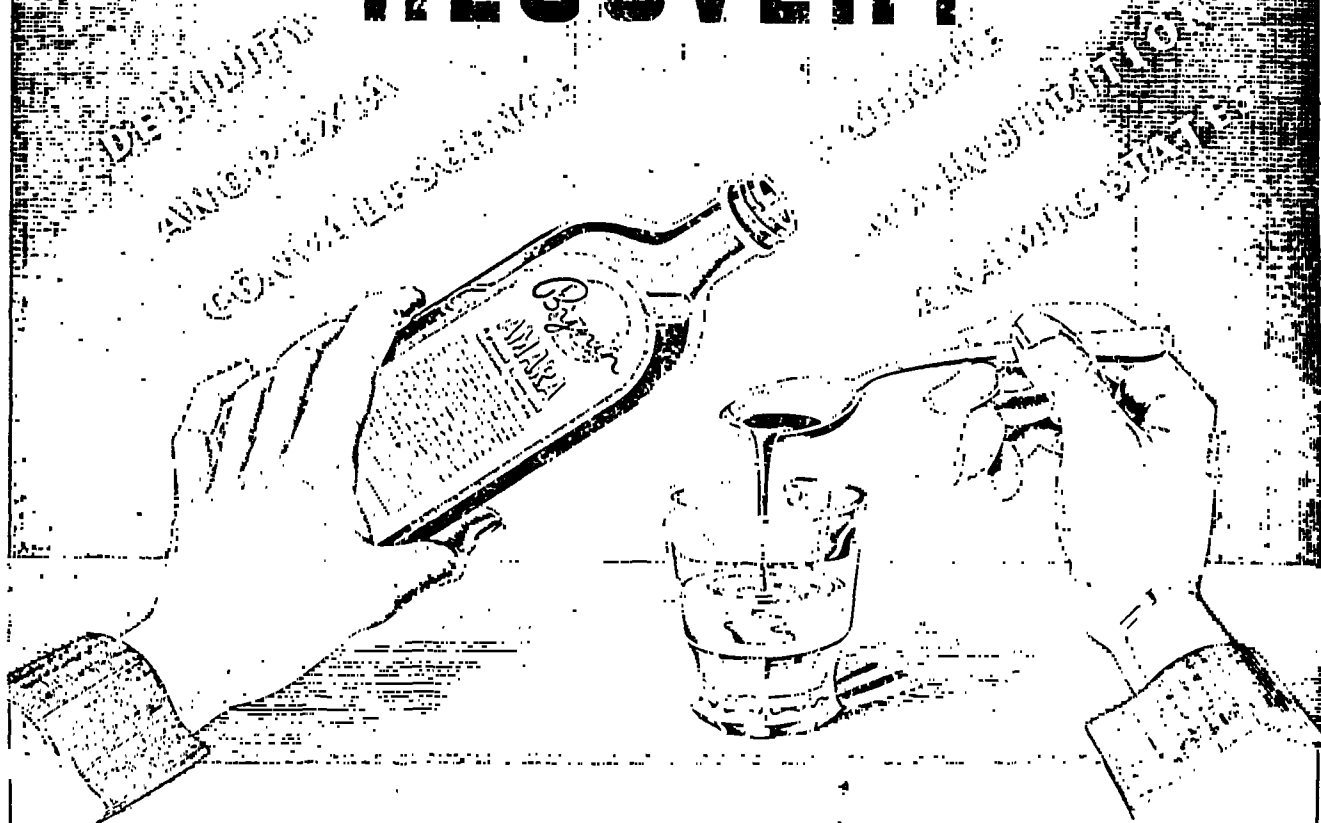
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Unless otherwise stated, the dosage mentioned is that for adults. In recommending the use of a single dose of 300 mg. paludrine for the treatment of the febrile attack in semi-immunes and a weekly dose of 300 mg. for suppressive purposes, the advantages of these procedures are emphasized as (1) bringing an effective antimalarial drug with the economic capacity of village and rural populations of endemic areas of malaria, and (2) providing a method of prophylaxis easy of administration.

Treatment of Neurosyphilis with Combination of Malaria and Penicillin

By R. R. KIERLAND *et al.*

(From the *American Journal of Syphilis, Gonorrhœa and Venereal Disease*, Vol. 32, September 1948, p. 470, as abstracted in the *Journal of the American Medical Association*, Vol. 139, 22nd January, 1949, p. 254)

KIERLAND and his co-workers treated 76 patients, 59 men and 17 women, the majority of whom were aged 40 or more, who had severe neurosyphilis, with a combined course of malaria and penicillin. Spinal fluid examinations reveal that 40 of the 76 patients had the most active and abnormal fluids before treatment, while 1 patient was classified similarly when last examined. 'Arrested' type of spinal fluids was observed in 4 patients before malaria-penicillin treatment, while 48 patients had similar findings after treatment. Sixty-seven patients had minimal abnormalities, arrested condition or normal fluids after treatment. In general a higher percentage of parietic patients had abnormal reactions following treatment than of any other group. Three patients had a relapse in the cell count after an initial return to normal. The clinical response was satisfactory in 44 of the 63 patients who had symptomatic neurosyphilis before treatment, and 4 of these 63 patients were clinically worse than before treatment. Only 3 of 7 patients with symptomatic optic atrophy had some improvement of vision, while 28 of 35 patients with symptomatic paresis and taboparesis had satisfactory clinical responses. The lapse of time seemed to improve the clinical results. Part of this apparent improvement was due to the selection of some cases earlier for further treatment because of incomplete response to initial therapy. Combination of malaria and penicillin is the treatment of choice in severe parenchymatous types of neurosyphilis. Patients with the milder forms of neurosyphilis, such as asymptomatic and meningeal syphilis, may first be given the advantage of one or two courses of penicillin alone.

Treatment of *Filaria bancrofti* with Hetrazan

By J. OLIVER-GONZALEZ *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 139, 29th January, 1949, p. 308)

THIRTEEN (56.5 per cent) of 23 persons with microfilariæ of *Wuchereria bancrofti* were found free of the infection as evidenced by negative microfilarial counts performed fifteen months after treatment with hetrazan (1-diethyl-carbamyl-4-methylpiperazine hydrochloride). The remaining 10 had very low counts, which had persistently remained at low levels since the end of the course of treatment. There was no increase in the number of microfilaria during the follow-up period in any of the patients which might suggest a relapse.

In general, the patients who received the highest total doses were the ones with negative smears at the

end of the fifteen-month period. The others probably did not receive sufficient amount of the drug to eradicate the infection entirely. All but one of the group of 23 patients remained symptom-free. None of the patients showed evidence of disease in their lymphatic or other systems suggesting clinical filariasis.

These observations would seem to indicate that hetrazan, when given in adequate dosage to patients infected with *W. bancrofti*, cleared the blood stream of microfilaria for periods of at least fifteen months.

The Treatment of Acute Peritonitis

By W. A. ALTEMEIER

(Abstracted from the *Journal of the American Medical Association*, Vol. 139, 5th February, 1949, p. 347)

A REVIEW of our clinical experience during the past six years with 598 cases of acute septic peritonitis secondary to acute appendicitis, perforated peptic ulcers and penetrating wounds of the abdomen indicates that successful management depends primarily on early diagnosis and good surgical intervention and secondarily on chemotherapy and adequate supportive treatment. There is no specific therapy for this infection as yet, and chemotherapy is not a substitute for prompt diagnosis and early operative repair or removal of the primary source of infection before abdominal distension, intestinal stasis and cardiovascular depression have occurred.

A comparison of the results obtained in 685 similar cases treated without chemotherapy with those in cases in which chemotherapy was used reveals that the mortality has been reduced approximately 60 per cent recently and that this reduction is apparently due to the effects of chemotherapy.

The most effective chemotherapy in our experience is obtained by the combined parenteral administration of sulphadiazine and penicillin or that of penicillin, sulphadiazine, and streptomycin. When used alone in a high dosage of 100,000 to 500,000 units every two or three hours, penicillin is effective in the great majority of instances, with the exception of those infections caused in part by virulent Gram-negative bacteria.

A review of our previous experimental work suggests that the unexpected effectiveness of penicillin in acute septic peritonitis is the result of a conversion of a severe synergistic and mixed infection into a simpler one produced predominantly by Gram-negative bacteria, usually of low virulence. The combined use of sulphadiazine and/or streptomycin with penicillin is recommended for the further control of this ætiologic component of peritonitis.

Treatment of Brucellosis with Streptomycin and a Sulphonamide Drug

By W. W. SPINK *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 139, 5th February, 1949, p. 352)

THE simultaneous administration of streptomycin and a sulphonamide, especially sulphadiazine, has been utilized in the treatment of 23 patients with brucellosis over a period of fourteen months. It is recommended that 0.5 gm. of streptomycin should be injected intramuscularly every six hours for a total of 28 gm. given in fourteen days. At the same time that treatment with streptomycin is begun, an initial dose of 3 to 4 gm. of sulphadiazine is given orally and then 1 gm. every four hours for at least fourteen days. One of the doses of sulphadiazine may be omitted routinely during the night.

The foregoing type of combined therapy has been followed by a relatively low number of relapses; toxic reactions to either drug have not been serious, and the appearance of *Brucella* has not occurred. *Brucella* has proved effective in the febrile and bacteraemic patient, with and without complications, its effectiveness in the obscure and indolent forms of chronic brucellosis require further investigation.

Investigations on Antibilharzial Action of Miracil D (Nilodin)

By J. M. WATSON *et al.*

(From the *Transactions of the Royal Society of Tropical Medicine and Hygiene*, Vol. 42, July 1948, p. 37, as abstracted in the *Journal of the American Medical Association*, Vol. 139, 5th February, 1949, p. 415)

Watson and his co-workers review the history of attempts to develop a drug for the oral treatment of bilharzial disease in human beings and give an account of the development of the new antibilharzial drug 'miracil D' ('nilodin'), which is a thioxanthone derivative (1-methyl-4-diethylamino-ethylaminothioxanthone hydrochloride). In those animals to which a sufficient dosage was given over a sufficient length of time, both viable ova and the symptoms of the disease disappeared and at necropsy only dead and disintegrating worms were found. In lower dosages the drug killed some of the worms and cured some animals, but not others. In human beings with bilharzial disease, low dosages appeared to be erratic in action, curing some patients and failing to cure others, but the results of the later trials, in which higher and more frequent doses were given, were more consistent. Viable ova disappeared from the urine or faeces, haematuria vanished and the physical condition of the patient substantially improved, but most cases later showed partial relapse. Further improvement was achieved after second treatment, and although few complete cures were obtained, the reduction in the number of ova and the amount of blood in urine or faeces was considerable. The minimum effective dosage seemed to be 5 mg. per kilogram every twelve hours for a minimum period of five days, although a higher rate is almost certainly desirable. Toxic symptoms are generally slight and appear to affect only 1 out of 5 or 6 patients.

Glycerine Osmotic Drainage in Peritonitis

(Reproduced from Surgical Newsletter No. Wa-161 dated July 1949 prepared by the American Medical Association)

The Smiths say that in a previous paper one of them advocated the intraperitoneal use of glycerine as an osmotic and antiseptic agent in peritonitis. They now offer their evaluation of glycerine osmotherapy after using it in the treatment of peritonitis for over ten years.

The technique of intraperitoneal glycerine osmotherapy varies with the extent of the infection. With localized soiling, as from a gangrenous gallbladder or appendix, without wide diffusion of peritonitis, a glycerine swabbing of the contaminated area and the insertion of a Kehrer cigarette drain, the gauze of which has been saturated with glycerine, is all that is needed. When one encounters diffuse peritonitis, with agglutination of intestinal loops and pocketing of pus, a more generous use of glycerine is indicated. The loops of intestines are gently separated to permit aspiration of pus collections and free lavage with glycerine. As much as eight ounces of autoclaved

U.S.P. glycerine is poured over the inflamed intestines and at least one osmotic drain is placed in the crater of the infection. Unlike normal peritonium, an oedematous wound is not irritated by full strength glycerine since fluids extracted from the tissues seem to dilute the glycerine in contact with the serous membrane.

The authors present a few case reports to illustrate the possibilities of osmotherapy in patients desperately ill with diffuse peritonitis.

In the concluding summary the authors stress that laboratory investigation and clinical experience indicate that glycerine has several useful properties which make it suitable for intraperitoneal use in the treatment of acute diffuse secondary peritonitis:

1. By osmosis, glycerine induces drainage from infected tissues.
2. It has an extended antiseptic and an adequate bactericidal action on the ætiologic bacteria of peritonitis in concentrations that do not prevent normal functional activity of the body cells.
3. By limiting the extent, and shortening the duration, of infection it tends to restrict the formation of residual adhesions.
4. Glycerine absorbed from the peritoneum has a protein-sparing action, reduces hypoglycaemia and prevents formation of acetone bodies.
5. It causes an increase in the number of leucocytes and their protective localization within the abdomen.
6. Used in conjunction with a mechanical drain it prevents the latter from adhering within the abdomen and avoids the skin maceration and superficial infection usually associated with prolonged pus drainage.

(Smith, E. D., Owensboro, Kentucky, and Smith, R. W.: *Southern Surgeon*, 15, 18-28, January 1949. The authors are connected with the Owensboro-Daviess County Hospital, Owensboro, Kentucky.)

Examination of New Habit-Forming Drug

(Abstracted from the *Chronicle of the World Health Organization*, Vol. 3, No. 2, February 1949, p. 27)

MANY new synthetic anæsthetics and analgesic drugs, for use as substitutes for morphine, have been evolved in the past few years. The question now arises whether these drugs will prove to be habit-forming.

After considering the reports submitted by experts on each of the drugs under examination, the WHO expert committee recommended that the following substances and groups of substances be brought under the existing international conventions on account of their habit-forming potentialities:—

Valbaine.

Metopon hydrochloride (methyldihydromorphinone hydrochloride).

Acetylcodeone (acetyldihydrocodeine hydrochloride).

Dolantin (Demerol, Pethidine, Piridosol) (1-methyl-4-phenyl-piperidine-4-carboxylic acid ethyl ester).

Methadone (Amidone).

*Heroin (diacetylmorphine).—*The committee expressed its alarm that although the dangerous nature of heroin is now universally recognized, consumption of this drug has increased considerably in certain countries. Heroin is known to be more toxic than morphine, as its analgesic effect is from four to eight times more powerful. Its effect on the nervous system is much greater and 0.007 g. of heroin is sufficient to induce respiratory paralysis. Over the last fifty years, heroin has caused great havoc in the world. It is strange to note that in some countries heroin continues to be widely prescribed, while others have completely ceased to use it. The committee was of the opinion that further

information was urgently needed on the reasons for the continued use of considerable quantities of heroin in some countries.

Finally, the committee was impressed by the variety of names given to the same drug by different manufacturers. Indeed, to avoid ambiguity, it had been necessary to give the full chemical formula of these substances. The committee drew attention to the advantages which would result if each substance could be given a recognized name by some authoritative, and preferably international, body.

Intra-Arterial Transfusion: Experimental and Clinical Considerations

(Reprinted from Surgical Newsletter No. Wa. 178 dated September 1949 issued by the American Medical Association)

In the light of previous work it appeared to Robertson and his associates that intra-arterial transfusion could be of value in the treatment of shock. The transfusion of blood intra-arterially is based upon the hydraulic principles of Archimedes. Under a pressure greater than that of the mean arterial blood pressure an infusion will enter the arterial system. The increased pressure and flow will be conducted throughout the entire system, as far proximally as the aortic valves. There will be an immediate increase in arterial pressure and blood volume. Under the conditions of shock, in which there is a lowered blood pressure, decreased blood volume, and reduced tissue perfusion, an intra-arterial infusion will act to restore to normal levels all three deficiencies.

The authors describe a method for the rapid administration of blood intra-arterially with experimental observations and report of its clinical application in 12 patients.

The results of their experimental and clinical use of blood transfusion by the intra-arterial route have substantiated the premise upon which the earlier investigators worked; that is, an immediate and sustained response is effected, with rapid rise in blood pressure and restoration of blood volume.

Administration of blood by this method is indicated primarily in the treatment of shock resulting from a rapid decrease in blood volume, severe traumatic shock which fails to respond adequately to conventional therapy, exsanguination in obstetric emergencies, intra-abdominal and intra-thoracic hemorrhage. Anesthetic emergencies and asphyxia may also respond to intra-arterial transfusion. It is recommended that other measures to combat shock or hemorrhage, such as the administration of stimulants, oxygen, intravenous infusion and transfusion, be used simultaneously.

Intra-arterial transfusion involves the sacrifice of an artery, and is a procedure which should be reserved for extreme emergencies after conventional methods of therapy have failed to effect a satisfactory response.

This procedure does not lend itself to the treatment of terminal stages of acute or chronic disease in which a response might be only transitory, as demonstrated in two cases in which the patients died after an initial response to the transfusion. The wisdom of an intra-arterial transfusion in the presence of heart disease or heart failure is debatable.

Active bleeding from a wound, peptic ulcer or traumatized organ is not in itself a contra-indication for intra-arterial transfusion, provided there is a possibility of control of the hemorrhage. It is obvious, however, that with this, as with any other procedure to replacement of blood, continued or recurrent hemorrhage will vitiate whatever improvement has occurred.

(Robertson, R. L., Atlanta, Ga., Trincher, I. H., and Dennis, E. W.: *Surgery, Gynecology and Obstetrics*, 87, 695-704, December 1948. The authors are connected with the Department of Surgery, Emory University

School of Medicine, and the Surgical Services, Grady Memorial Hospital and Emory University Hospital.)

Treatment of Tetanus

(Reprinted from Surgical Newsletter No. Wa. 178 dated September 1949 issued by the American Medical Association)

According to Smathers and Weed the control of tetanic muscle spasms and neutralization of the toxin are the chief objects in the treatment of tetanus. The authors formulate a plan of treatment which is based on a review of 86 cases of tetanus from three Detroit hospitals. Special attention is given to recent cases in which 'intocostin' and d-tubocurarine in wax and oil were used.

The plan of treatment is divided into three phases: pre-operative, operative and post-operative. The patient on admission is immediately given a cutaneous test and conjunctival test with tetanus antitoxin diluted 1 : 100. If sensitivity is present, desensitization is attempted or 'despeciated' antitoxin is given if available. If a wound can be found, 50,000 units of antitoxin is given intravenously and 10,000 units locally around the wound. If no wound is found, the entire contents of three 20,000 unit vials is given intravenously.

As soon as the sensitivity test is given, 1 cc. of d-tubocurarine in wax and oil is administered intramuscularly. For immediate control of convulsions, 'intocostin' may be given intravenously, but the authors prefer to remove the patient to the operating room at once for ether anesthesia. In the operating room, with the patient anesthetized, 20,000 units of tetanus antitoxin is injected intrathecaally and the wound debrided.

Post-operatively the patient is returned to a darkened private room with a special nurse. Available at the bedside are nasal oxygen, a laryngoscope, an endotracheal tube and aspirating apparatus. Appropriate medication for rest is ordered. Penicillin is given every three hours to prevent infections of the respiratory tract and for its action on infected wounds. Penicillin, although it is said to have a bacteriostatic effect on *Cl. tetani*, has no apparent effect on the toxin produced and no proved clinical effect in the treatment of generalized tetanus.

Five thousand units of tetanus antitoxin is given daily to neutralize any additional toxin that may be absorbed. This is continued for five days if the infected focus has been removed, longer if the focus cannot be found.

D-tubocurarine in wax and oil is given intramuscularly daily according to the clinical response of the patient. Relief of spasm can be obtained without the production of laryngeal or diaphragmatic paralysis. Patients who receive this medication must, in the present state of our knowledge, be watched constantly by experienced personnel in order that any evidence of curare toxicity may be coped with immediately.

(Smathers, H. M., Dearborn, Mich., and Weed, M. R.: *Archives of Surgery*, 57, 291-300, September 1948. The authors are connected with the Department of Surgery, Wayne University College of Medicine and the Detroit Receiving Hospital, and the Department of Medicine, Wayne University College of Medicine.)

Consideration of Management of Child with Rheumatic Fever

By A. E. HANSEN

(Abstracted from the *New Orleans Medical and Surgical Journal*, Vol. 101, December 1948, p. 264)

The four phases of management, regardless of the total duration, may be considered as follows:

Acute—keynote—bed rest and symptomatic therapy.

Subsiding—keynote—diet and restriction of activity.
Convalescent—keynote—diet and graduated physical activity.

Quiescent—keynote—prevention of recrudescences.

ACUTE PHASE

Pain, fever and other acute symptoms

Strict bed rest—to assist in this, sedatives such as phenobarbital may be helpful.

Salicylates—sodium salicylate or acetyl-salicylic acid, 0.10-0.15 gm. per kilogram (grain per pound) body weight daily in divided doses four times per day. It is important to watch closely for signs of salicylate intoxication—the first sign usually being hyperpnoea from central nervous system stimulation. Acidosis may develop even before such symptoms of salicylism as tinnitus and vomiting are very marked.

Oxygen—more and more it is developing that in the presence of carditis liberal use of the oxygen tent is helpful in reducing cardiac damage.

Diet—every effort should be made to maintain good nutrition using frequent small attractively prepared meals.

General supportive measures—pleasant environment, psychological reassurance, and mild entertainment preferably with no visitors; and body comfort such as removal of weight of bed clothes from painful joints. Seldom is it necessary to employ local heat, flannel wrappings, or methyl salicylate in oil.

Chorea minor

Bed rest—with padding of hard surfaces for protection from injury. Quiet environment.

Sedation—very satisfactory is phenobarbital, 0.032 to 0.045 gm. three to four times daily until drowsy then decrease somewhat. Innocuous rashes develop occasionally. Other sedatives may be tried.

Diet—it is important to assist in the feeding of these children, and extra efforts, though time consuming, must be made.

Fever therapy—may be used in the severe cases.

Cardiac decompensation

Strict bed rest—with liberal use of sedatives, even employing narcotics.

Oxygen tent—continuous.

Diet—low sodium with frequent small feedings.

Diuretics—employment of theocalcin or mercurhydrin.

Digitalis—use is controversial in the cardiac failure associated with acute rheumatic disease; however, it may be tried using Eggleston dosage. Electrocardiograms should be taken to check for digitalis intoxication.

SUBSIDING PHASE

Bed rest until rheumatic activity subsides.

Nutritious diet with liberal use of iron and vitamin supplements.

Diversional therapy—mild play activity in bed and later simple occupational tasks.

Emotional and psychological conditioning.

General supportive measures with limited visitors allowed.

CONVALESCENT PHASE

Graduated physical activity—it is well to plan a positive schedule. Actually such activity begins in the subsiding phase, however, individuality is the keynote with one-half to three weeks between each step in the following schedule:

Feed self—toys in bed—holding books.

Sit up in bed—fifteen minutes, then thirty minutes, once then twice daily.

Bathroom privileges—once then twice.

Diversional therapy—quiet games and reading.

Sit in chair—fifteen minutes then thirty minutes, once then twice daily.

Meals with family—first, dinner, lunch, then breakfast.

Walk about house—fifteen to thirty minutes once then twice daily.

Out of door walking—fifteen to thirty minutes once then twice daily.

Limited school work at home.

Climb stairs once then twice daily.

Rest period—one hour in morning and two hours in afternoon—later one per day.

School—one or two classes—then half day—then all day with rest periods during and after school.

This whole activity programme may be weeks to months if no carditis, or months to years if carditis is severe.

Diet—continue with good nutritional programme.

Education—planned according to disability—present and prospective.

Physical therapy—play, occupational and diversional programme according to ability and reaction to increase in exercise.

Psychological and emotional conditioning—it is important to assist in keeping up morale and avoid allowing 'do not do that' or 'don't do this', and 'remember your heart' to become the chief conditioning statements. Such admonitions go far towards developing 'induced invalidism' which should be rigorously avoided. An optimistic cheerful attitude must be assumed.

Environment—insofar as possible favourable hygienic conditions and pleasant surroundings should be provided. Favourable climatic conditions are of assistance. In many instances this may be provided in the patients' own home, but in some places superior convalescent homes with complete programmes are available.

Removal of foci of infection—foci in teeth, sinus, and tonsils should be investigated, and these should be treated. In the event operative procedures are to be carried out, sulphonamide or penicillin seems to be especially helpful in preventing the blood stream invasion hence prevents the development of subacute bacterial endocarditis. It should be pointed out that removal of tonsils and adenoids is not effective in preventing subsequent attacks of acute rheumatic fever.

QUIESCENT PHASE

In general the same rules presented under Convalescent Phase are applied during this phase in regard to diet, physical activities, psychological conditioning, and educational and occupational programmes. Particular emphasis is placed on the prevention of recrudescences. Measures which have been used are: Prolonged care in convalescent home, removal to a favourable climate, salicylate administration for a month when afflicted with hæmolytic streptococci group A infection of the throat; and periodic injections of tannic acid precipitated hæmolytic streptococcal toxin. Penicillin has not been given any more than a preliminary trial. Particularly successful has been the continuous daily administration of sulphonamides to those individuals likely to develop recurrences of rheumatic infection.

When all signs of rheumatic activity have disappeared such drug as sulphadiazine or sulphamerazine 0.5 gm. may be given with breakfast and supper to those over ten years of age and 0.25 gm. twice daily to those under ten years. For the first week, one-half the expected daily dose may be given. Periodic examinations of the patients should be made for the first four to six weeks at weekly intervals and later at four to

Vitamin Therapy—its uses and limitations

DEBILITY IN CONVALESCENCE

Modern work indicates that this state is due in no small measure to sub-normal nutrition from restricted food intake and increased utilization of nutrients during illness. There is much to support the view that many symptoms of such debility are manifestations of hypovitaminosis. Thus deficiency of the vitamin B complex may be shown by anorexia, lassitude, mental and physical fatigue, atonic gastro-intestinal disturbances, constipation, irritability and nervousness, all of which may be present in the debilitated state.

To restore depleted reserves of vitamins and maintain an optimal level, the debilitated patient frequently needs a prolonged course of vitamin therapy.

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		protein	30%		

References:—Shortage of space precludes list of references, but full documentation may be obtained on application to:
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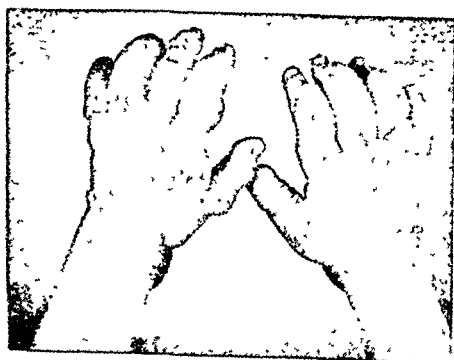


Fig. 1

BADLY SCALDED HANDS

12th November, 1947. 10.45 a.m. (M. C.) age 4, immersed her hands in nearly boiling water.

12.40 p.m. Admitted to hospital.

General Condition: Agitated and screaming but not shocked.

Local Condition: Commencing blister burns of entire surface of both hands. Covered with sterile towels and admitted Burns Unit at 1.02 p.m. Stopped screaming and given Omnopon gr. 1½, Scopolamine gr. 1/600 at 2.30 p.m. Plenary Dressing 3.45 p.m. On examination Rt. and Lt. hands. Scalding of entire surface of both hands and wrists, large blisters and much oedema. (Fig. 1.)

Treatment: Cleaned with 1 per cent. Cetavlon, dressed with Penicillin Cream 400 units per gram, gauze, wool, crepe bandages and Gypsona P.O.P. over massive dressings. Admitted to ward with both hands elevated. (Fig. 2.)

General condition satisfactory but slight pyrexia for 48 hours until 21st November, when Penicillin dressings and Gypsona were renewed. Rt. hand very satisfactory. Lt. hand healing slowed due to mild infection.

25th November. Rt. hand continues improving. Lt. hand, still some discharge. Entire dressing renewed.

9th December. After further re-dressings with Penicillin and Tulle Gras movement. (Fig. 3.)

17th December. Discharged.

22nd June, 1948. Review. Shows 100 per cent. functional and cosmetic recovery.

These details and illustrations are of an actual case.

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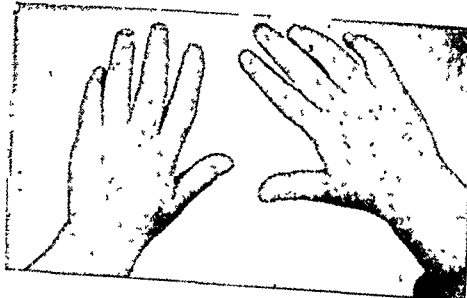


Fig. 3



Fig. 2

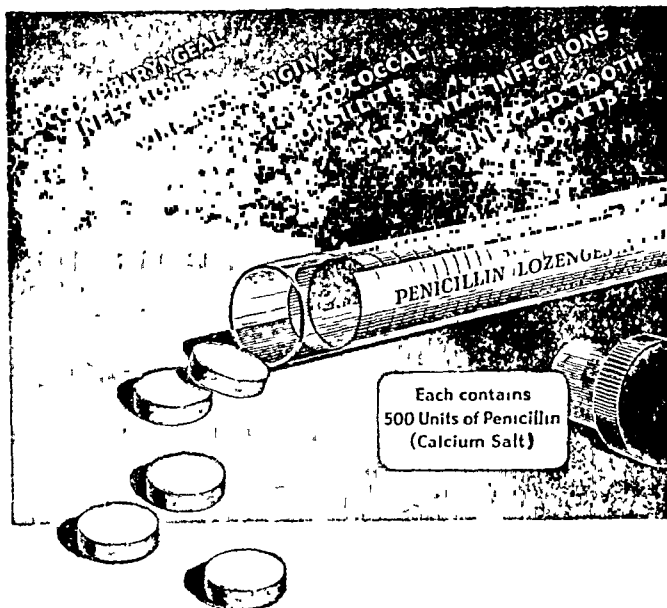
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six weeks intervals. The haemoglobin, leucocyte, and differential white cell count, and blood sulphur levels, as well as urine examinations should be made. The patient should be kept under continued surveillance. It has not been determined as to how long such a regime should be carried on. Inasmuch as 80 per cent of the recurrences develop within five years, it would seem that this should be the minimum interval. Furthermore, the likelihood of recurrences before and after 15-16 years of age are 5 : 1. Therefore, it would seem that children should be kept on such a prophylactic programme until after puberty.

Prohibition and Health

By M. C. NAMBUDIRIPAD

(Abstracted from *Current Science*, Vol. 18, May 1949, p. 166)

THE September 1948 issue of *Current Science* contains a masterly leading article on the 'Scientific and Economic Aspects of Prohibition'. But, I am afraid, some important health problems arising from Prohibition have been overlooked in the article. True, 'drink devil' has become a problem and a menace in regard to the health of the community. But, strangely enough, prohibition too will bring in its train a number of important health and nutritional problems, which the scientist and the administrator will do well to study.

In his book, 'The Inequality of Man', Prof. J. B. S. Haldane, F.R.S., draws attention to the 'Tragedy of Nauru', an account of which appeared in the *Proceedings of the Royal Society of Medicine* (1930).

'Nauru or Pleasant Island lies in the Pacific Ocean near the equator and contains large deposits of phosphate. So its inhabitants contribute to the world overproduction of food (Haldane refers only to the food situation in 1930) by exporting portions of their native land. They were in the habit of drinking toddy made from fermented palm-juice and on occasions became very tipsy in consequence, which doubtless lessened their efficiency as excavators. Nauru is governed by Australia under a mandate from the League, and the paternal Government issued an ordinance forbidding the issue of toddy. Perhaps the efficiency of the natives as labourers increased, but their infantile mortality rose to 50 per cent within six months of this law coming into force.

'It was found that the children at the breast were dying of beri-beri, a disease due to the deficiency of vitamin B₁. This substance is nearly absent from the rather monotonous diet of the mothers, but is present in large quantities in the yeast from which the toddy is made. The Medical Officer of Health discovered this fact and (doubtless after an appropriate delay) toddy was allowed again. The infant mortality immediately fell to 7 per cent.

'This situation in many areas of Central India is quite similar. Large sections of the population are on the border-line of vitamin B₁ deficiency, and suffer from time to time from mild beri-beri. In these circumstances, adults generally survive in rather poor health, but breast-fed children die. This dietary deficiency is at least to some extent supplemented by the use of toddy made from palm-juice' (Haldane).

Prohibition of distilled drinks, such as arrack and imported varieties, is quite welcome. Those drinks have no food-value and they do irreparable harm. But, prohibition of crude toddy takes away from the hands of the ordinary labourer his only source of vitamin supply. The well-to-do members of the community invariably go in for 'costly drinks', which means distilled ones. Even if some of them have been using crude toddy, before the introduction of prohibition, they can now afford to turn to costlier ways of fighting

vitamin deficiency. To the common labourer, no such alternative exists.

It is therefore the duty of the Government to look into this matter at once.

Studies on Indian Edible Oils: Ground-Nut Oils

By K. RAMAMURTI

and

R. N. BANERJEE

(Abstracted from the *Indian Journal of Medical Research*, Vol. 36, October 1948, p. 371)

THE nutritive value of a fat can be considered from several points of view. To serve as food, its assimilation and utilization in the metabolism are important. The first process, therefore, is digestion; while absorption comes later. Oils and fats are the carriers and solvents of vitamins and carotenes. The rôle of Indian edible oils in this aspect of the problem is vital for the health of the nation. The digestibility of the carotenoid foods and their retention is a great criterion in the tropics more so with the vegetarians of India. In a tropical country like India, oils and fats quickly go rancid, unless consumed, soon after their preparation. Therefore, this storage property is very important. In the cooking processes of frying, etc., the oil is exposed to high temperatures when oxidation and peroxide formation take place.

The Report of the Marketing Board on Ground-nut Oil gives a picture of the uncontrolled state of affairs and bad quality of the oil put on the market. The development of acidity on storage of nuts in Bombay and Madras has been recorded. The development of acidity has been found to be considerably increased by 'damaged', 'splits' and 'nooks'. Nothing is done by the crushers before extracting the oil; so that, oils with very high acidity are produced. No limit has been prescribed for the free fatty acidity of the oil that can be considered fit for edible purposes. Only hydrogenation factories refuse oils above a certain acidity and colour as it adds to their cost of manufacture and affects the yield. The Agmark has given no specifications for good quality edible oil. This is a deplorable state of affairs since high acid and rancid oils are known to destroy vitamins. It is, therefore, very important that a limit be prescribed for the acidity in edible ground-nut oil.

From the point of view of digestibility, storage property, and as carrier and solvent for carotene and vitamin A, ground-nut oil below 1 per cent free fatty acidity alone should be considered suitable for edible purposes. Removal of acidity or refining a high free fatty acidity oil fails to bring it to the quality of fresh low free fatty acidity oil. Any oil of over 2 per cent acidity should be rejected for edible purposes. Gallates, especially progallin A (ethyl gallate), increase the storage property 2 to 4 times.

Poisoning by Vegetable Laxative Pills

(From the *New Zealand Medical Journal*, Vol. 48, April 1949, p. 166)

THE danger to young children of sugar-coated tablets was once again demonstrated by the death of a female child of 14 months in the Wellington Hospital on 15th October, 1948.

The circumstances of the child's death were the subject of an enquiry by the Wellington Coroner, Mr. W. G. Mellish. The child was playing about the house with an older brother.

was given a bottle of pills. The younger child was able to unscrew the cap of the bottle and swallowed the contents. The mother had had the pills for some considerable time and as far as she could remember there were no more than 10 or 12 pills in the bottle. The child's mother quickly discovered what had happened, gave the child an emetic of salt and water, which resulted in several of the pills being vomited. In spite of these measures, however, the child became ill and at 8 p.m. the same evening was admitted to hospital. Its stomach was washed out there without much result. During the night the child showed signs of circulatory collapse and died at 7 a.m., approximately 16 hours after taking the pills.

There was little to be found at post-mortem examination except deep congestion and cedema of the brain. There was a quantity of dark material in the stomach and jejunum but there were no signs of irritation.

The pills were found on analysis to be the vegetable laxative pill of the British Pharmaceutical Codex—*Tabella Leptandræ Gomposita*—the poisonous ingredients of which are extract of colocynth, of which there is one grain in each tablet, and extract of hyoscyamus, of which there is $\frac{1}{2}$ grain in each tablet.

The case is reported as illustrating the danger to children of pills which are usually regarded as being relatively harmless.

Malaria Simulating Acute Appendicitis

By A. B. MORALES *et al.*

(Abstracted from the *Journal of the Philippine Medical Association*, Vol. 25, March 1949, p. 135)

1. Six patients with malaria are presented, to illustrate our observation that intestinal malaria may be confused with acute appendicitis.

2. The occurrence of moderate or high fever before other signs and symptoms, a positive history of previous attack of malaria, a palpable spleen, and a normal white blood cell picture or leucopænia, are strongly suggestive of malaria, even when the abdominal signs and symptoms indicate a pathology in the terminal ileum, cæcum and appendix. Our diagnosis of intestinal malaria in all our six cases were confirmed by positive blood smear and therapeutic tests.

3. Authorities are unanimous in their observation that, in some cases of malignant malaria, the capillaries of the mucosa and villi of the intestines may be plugged with parasites. The intestines are also congested.

4. The pain, tenderness, and hyperæsthesia at the right iliac region in cases of bacterial and protozoan affections of the terminal ileum, cæcum, and appendix are explained as referred visceral sensations.

5. While Manson Bahr observes that only malignant tertian malaria simulates surgical conditions, one of our patients, with signs and symptoms similar to those of acute appendicitis, harboured benign tertian parasites.

Preliminary Report on the Beneficial Effect of Chloromycetin in the Treatment of Typhoid Fever

By T. E. WOODWARD *et al.*

(From the *Annals of Internal Medicine*, Vol. 29, July 1948, p. 131, as abstracted in the *Bulletin of Hygiene*, Vol. 24, January 1949, p. 16)

WHILE studying the effect of chloromycetin on scrub typhus in Malaya, the authors also had the opportunity of treating 10 cases of typhoid fever: the drug was given orally in doses of 0.25 gm. first at intervals of

2 hours, and after the temperature had fallen, at intervals of 3 or 4 hours. The concentrations so produced in the blood were found to be 40 to 80 μ gm. per ml. in the first stage and 20 μ gm. subsequently (*Salmonella typhi* is inhibited *in vitro* by about 0.25 μ gm. per ml.). Improvement was usually evident within 24 hours and the temperature often normal after 3 days (average 3.5, and for 8 control cases 26 days, reckoned from the 9th day, this being the mean duration of fever before treatment was begun). Frequent blood cultures were all sterile, having been positive in each case before treatment. Two patients had relapses with bacteræmia which responded promptly to further treatment: one had a perforation and one a severe hæmorrhage, in each case while afebrile. Both recovered: one of the controls died. Stool cultures were positive in 2 patients during convalescence, but only for short periods (up to the 12th and 17th days after treatment began).

Studies of the Acute Diarrhœal Diseases. XX. Further Observations of Chemotherapy in Shigellosis: The Efficacy of Streptomycin and Sulphacarzole

By A. V. HARDY

and

S. P. HALBERT

(From the *Public Health Report*, Vol. 63, 11th June, 1948, p. 790, as abstracted in the *Bulletin of Hygiene*, Vol. 24, January 1949, p. 16)

IN this paper are recorded the results of treatment of Flexner dysentery in 37 patients with streptomycin, in 10 with sulphacarzole, and in 10 with sulphadiazine. As a control 10 patients were untreated. All were mental defectives aged between 5 and 15 years. In patients treated with streptomycin, and these included cases due to sulphonamide-resistant strains of shigellæ, the colony counts of both pathogenic and non-pathogenic organisms after plating of fæces rapidly decreased, so that by the 6th day after the beginning of treatment all cultures were negative for pathogens. They continued so for 3 days, but by the 14th day 6 of the 37 patients showed a recurrence of positive cultures. No significant toxic reactions to the streptomycin were encountered. The response to sulphacarzole, a poorly absorbed sulphonamide, was slow in comparison with streptomycin in reducing the fæcal plate count and one patient failed to give negative cultures after 14 days.

The reaction to sulphadiazine was very satisfactory and according to the tabulated data gave results superior to those obtained from the other remedies. All patients gave negative stool cultures by the third day and there were no recurrences. In the untreated series, 7 out of 10 patients were still giving positive cultures after 7 days, and 3 after 14 days. Although it is not explicitly stated, it would appear that sulphadiazine is the drug of choice for the treatment of Flexner dysentery and that streptomycin may be considered for infections caused by sulphonamide-resistant strains. The authors merely record that sulphadiazine was substantially more effective than the poorly absorbed compound sulphacarzole which 'had the weakness of other products of this type'.

Public Health Laboratory Service

(Abstracted from the *Bulletin of Hygiene*, Vol. 24, January 1949, p. 67)

THE paper gives details of the specimens required for the investigation of various infections and indicates the times at which positive and negative reports may be expected to be available.

The following list indicates the more usual specimens examined in different diseases (listed alphabetically):—

Conjunctivitis :

Swab of discharge and smears on glass slide.

Diphtheria :

Swab from infected throat, nose, ear, etc. In suspected carriers and contacts nose and throat swabs must both be taken.

Dysentery—diarrhoea of unknown aetiology :

Fæces. If specimens have to be obtained from large numbers of young children or child contacts of known dysentery cases, rectal (not anal) swabs may be taken, and must reach the laboratory within a few hours.

Enteric fever (typhoid and paratyphoid) :

Blood culture (5 ml.) in early stages: Blood (5–10 ml.) in a dry tube for Widal reaction (often negative in first week): appropriate containers supplied on request.

Fæces and urine from onset of symptoms.

Suspected carriers: consult laboratory.

Food poisoning :

Fæces: Vomit: Any portion of unconsumed suspected food.

Glandular fever (infective mononucleosis) :

Blood films: Blood in a dry tube for Raul-Bunnell reaction after first week.

Influenza :

Consult the laboratory or medical officer of health.

Malaria :

Thick and thin blood films.

Meningitis :

Cerebro-spinal fluid.

Pneumonia :

Sputum: Blood for culture or serological tests: Consult laboratory.

Puerperal fever :

High vaginal or cervical swab. For examination of contacts to trace source of infection, consult laboratory.

Pyrexia of unknown origin :

Blood culture: Blood in a dry tube for serological reactions: Blood films and white blood cell counts. Sputum when present: consult laboratory.

Skin and hair infections :

Swabs from skin lesion: Hair stumps or skin scrapings from suspected ringworm. It may sometimes be more convenient to send the patient to the laboratory.

Tonsillitis :

Nose and throat swabs.

Tuberculosis :

(a) *Pulmonary*: Sputum (not saliva) collected in the morning before food is taken. If one or more specimens are microscopically negative, sputum may be cultured.

(b) *Non-pulmonary*: Pus: Urine (morning specimen on 2 to 3 consecutive days or 24 hours' collection): Cerebro-spinal fluid.

Undulant fever :

Blood in a dry tube for serological tests (not positive in first week):

Blood culture when temperature is raised: consult laboratory.

Venereal diseases :

Gonorrhoea: Swab of discharge: smears on glass slides. Material for culture must reach laboratory within 1 to 2 hours of being taken unless

placed in containers with special preservative fluid; consult laboratory.

Wassermann and gonococcal complement fixation tests: Blood in a dry tube (5 ml.).

Vincent's angina :

Swab from lesion: smear on glass slide.

Weil's disease :

White cell count and blood films: Blood (5–10 ml.) in a dry tube for culture and serological tests.

Whooping cough :

Perinasal swab or cough plate: consult laboratory.

White cell count and blood films.

Special examinations :

Consult laboratory about specimens from uncommon diseases, e.g., actinomycosis, amœbiasis, anthrax, botulism, infective hepatitis, lymphocytic meningitis, poliomyelitis, rat-bite fever, smallpox, typhus fever, tetanus, worm infestations, etc.

Note.—1 millilitre (ml.) is approximately equal to 1 cubic centimetre (cc.).

Protein Value of Soya-Bean Milk : Human Feeding Experiments

By H. S. R. DESIKACHAR *et al.*

(Abstracted from the *Indian Journal of Medical Research*, Vol. 36, April 1948, p. 145)

WHEN cow's milk curd protein fed along with a poor South Indian rice diet is replaced by an equivalent amount of soya-bean curd protein, the mixed proteins of the diet in both cases are utilized to about the same extent.

Treatment of Bancroftian Filariasis with Hetrazan in British Guiana

By M. KENNEY

and

R. HEWITT

(Abstracted from the *American Journal of Tropical Medicine*, Vol. 29, January 1949, p. 89)

From the study of 296 cases of Bancroftian filariasis treated with Hetrazan in British Guiana the following conclusions and recommendations for treatment seem to be justified:

1. Rapid reductions in microfilariae are obtained when oral doses of from 0.2 to 2.0 mg. per kg. of Hetrazan are given three times daily. Most cases treated with 0.4 mg. per kg. or higher show negative counts one week after treatment has started, and these negative counts have been maintained generally for as long as follow-up examinations have been made (up to 4 months after cessation of treatment). Following doses approximating 0.2 mg. per kg. three times daily for 21 days or longer, the microfilariae may recur in small numbers at varying times after treatment has been stopped. This rarely occurs when higher doses are used. Very few cases are resistant to treatment.

2. The failure of microfilariae to recur in the peripheral blood after treatment has stopped in most cases indicates that the adult worms are dead or have been sterilized. It seems more likely that the adults are dead, since clinical improvement was obtained following acute exacerbations of filarial symptoms which we consider of allergic origin, and which are probably produced when filarial protein is released by dead worms.

3. Systemic reactions to Hetrazan itself are very mild and of short duration. Cases not sensitized to filarial protein rarely exhibit reactions of any sort during treatment. Headache, nausea, sedation and malaise are probably side-effects produced by Hetrazan itself, but these symptoms have never been severe nor long lasting.

4. Systemic reactions in clinical cases of filariasis during treatment with Hetrazan, particularly in cases with a history of severe filarial attacks, resemble filarial symptoms which occur in untreated patients. Nodular swellings, lymphangitis, pain in the abdominal region, temporary swellings of the extremities, and temporary aggravation of existing swellings, accompanied by fever and pain, occur with varying degrees of severity in clinical cases during treatment. Single or multiple manifestations occur at various periods after treatment is initiated. These have never reached alarming proportions, however, and in but extremely few cases has it been necessary to discontinue temporarily treatment or hospitalize patients because of reactions. In the few cases which were hospitalized, treatment was continued. It is difficult to explain these reactions in any way other than acute allergic phenomena brought about by the release of filarial protein in sensitized individuals. The total amount of protein released seems not as important as the relationship between the amount of antigen and the degree of sensitization of the individual.

The explanation of systemic reactions which sometimes occur during the treatment of this infection with Hetrazan on an allergic basis is further strengthened by the following facts:

(a) Patients infected with intestinal round worms or with no helminth infections whatever have never shown reactions other than those mentioned in item 3.

(b) Patients infected only with *Acanthocheilonema perstans* or *Mansonella ozzardi*, neither of which is affected by Hetrazan in doses effective against *W. bancrofti*, have shown no systemic reactions, even after prolonged courses of treatment.

(c) Patients infected with *Onchocerca volvulus* show systemic manifestations different in character and location from those occurring in *W. bancrofti*, suggesting that the site of the worms within the host governs the type and site of local reactions.

Despite the fact that symptoms during treatment have never reached alarming proportions, the possibility of severe allergic reactions should not be overlooked. It would probably be well to start treatment with low doses (0.2 to 0.5 mg. per kg.) in hypersensitized individuals with a history of unusually severe filarial attacks, although, as shown in the Kwakwani group, systemic reaction may occur during treatment with this dosage range. The possibility of alleviating the severity of some reactions by the use of anti-allergic medication should be considered.

5. The duration of dosage with Hetrazan in clinical cases cannot be based upon the rate of disappearance of microfilariae, because the dosage thus calculated may be sufficient to destroy microfilariae and the adult worms which produced them, but insufficient to kill worms which are screened by inflamed tissues and do not release microfilariae into the general circulation. Moreover, the duration of treatment cannot be determined by the complete disappearance of microfilariae from the blood stream, since it is believed that the effects produced against the microfilariae and the adult worms are distinct and separate. The optimal duration of treatment can be roughly estimated in clinical cases, however, by the time of appearance and disappearance of allergic reactions during treatment, since the reactions are thought to denote an effect against the adult worm. These symptoms occur at different times in different individuals. For maximum curative effects it is suggested that treatment be continued for at least 3 weeks after the disappearance of the last systemic reactions occurring during treatment.

This would bring the course of treatment to at least three weeks when the only reaction occurred on the first day of treatment, but in many cases further treatment would be indicated, since reactions might not occur and disappear until after one or more weeks of treatment. In cases of clinical filariasis where no reactions occur in the early period of therapy, it is more difficult to estimate the optimum duration of therapy. Such cases may not be sensitized to filarial protein when the adult worms are killed. On the other hand, the absence of any systemic reactions whatever may denote that the adult worms are not being killed, and periods of four to six weeks of therapy may be necessary.

6. Atypical clinical manifestations of filariasis, simulating malaria, arthritis, cutaneous diseases, etc., may be encountered in hyper-endemic regions. Since conditions of this sort frequently yield to treatment with Hetrazan they should not be overlooked.

7. In clinical filariasis, the absence of microfilariae in the blood is not a contra-indication for treatment; neither is the long duration of the infection nor the degree of elephantiasis. The improvement which occurred in more than 50 per cent of such cases after treatment with Hetrazan demonstrate that filariae were present, and that the death of the worms was followed by a recession of symptoms.

The Synergistic Action of Penicillin and Streptomycin on *Endamoeba histolytica* Cultures

By H. SENECA *et al.*

(Abstracted from the *American Journal of Tropical Medicine*, Vol. 29, January 1949, p. 37)

NEITHER penicillin nor streptomycin is amoebicidal in concentrations of 100 to 1,000 units per cc. A combination of the two, however, in equal unitage, kills amoebae in the first generation at a total concentration of 2,000 units per cc., and in the second generation at 1,000 units per cc. The latter concentration is found not to be bactericidal, hence the action is probably a direct one rather than an elimination of necessary bacterial products. Therapeutic application of the findings is suggested.

Death from Dicoumarol

(From the *Pharmaceutical Journal*, Vol. 162, 30th April, 1949, p. 322)

At Streatham, a 70-year-old woman died from hæmorrhage from the stomach and intestines caused by an excessive dose of dicoumarol.

On 7th March her medical attendant diagnosed a deep thrombosis of the left femoral vein. He prescribed glycerine of belladonna paint and dicoumarol, six tablets on the first day and thereafter four daily, and ordered her to bed. By 14th March she was restless and excitable. The use of the belladonna paint was therefore discontinued and the dose of dicoumarol was reduced to two tablets daily. She became worse, and on 26th March, the doctor having diagnosed renal colic, she was removed to hospital, where she died on 31st March. Altogether she had had about 48 tablets.

Giving evidence, the doctor said that the dose he ordered was that recommended by the makers. He also consulted the 'British Encyclopædia of Medicine'. He had had experience of the drug: he had used it in four previous cases in similar dosage, and in one case for 16 days without ill-effect. He did not remember

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For deep subcutaneous or intramuscular injections. Readily soluble in water. Available in ampoules of 0.10 gm. and from 0.15 gm. to 0.75 gm. in 0.15 gm. gradations.

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hearing of the danger of the drug or that its effect should be checked by examinations of the patient's blood.

The pathologist's report stated that there could be no doubt that the exhibition of dicoumarol had so reduced the prothrombin in the blood that hemorrhage had occurred from almost every surface. The effect of dicoumarol was somewhat cumulative, and persisted for some days after the drug was withdrawn.

A verdict of death by misadventure was returned.

Arachnidism: Effect of Calcium Gluconate in 6 Cases

By W. E. R. GREER

(From the *New England Journal of Medicine*, Vol. 240, 1949, p. 5, as abstracted in the *International Medical Digest*, Vol. 54, March 1949, p. 142)

'ARACHNIDISM, the syndrome following the bite of a black widow spider, is a definite clinical entity in the field of general medicine.'

'Although limited in practical application to regions where this spider is indigenous, knowledge of the clinical entity is important since many spider victims are subjected to needless operations because the symptoms often simulate acute surgical conditions of the abdomen. . . . The syndrome, as presented by 6 patients bitten by the black widow spider observed in a seven-day period in an overseas tropical area, usually followed a similar pattern: transient excruciating local pain at the site of the spider bite, rapid local oedema and redness of the skin at the site—in 2 cases the site could be identified; in 10 to 15 minutes a 'burning sensation' that spread centrifugally from the site of the bite and soon involved the whole body, passing off in about 20 to 30 minutes; a sudden

had normal or slightly elevated blood pressure); motion of extremities was limited by muscle spasm, and flexion was a prominent feature; the temperature was normal or only slightly elevated; the pulse was slow, being 80 or under in all cases; examination of the blood showed a moderate leukocytosis; and the 2 patients presenting a picture of profound shock showed albuminuria.'

'The victims all gave an excellent history, and in all cases the spider was identified.'

'The patients in this series were immediately given 10 cc. of 10 per cent calcium gluconate intravenously. Subsequently they were given a saline infusion containing 10 cc. of 10 per cent calcium gluconate. An ice bag was applied to the affected area. Relief was obtained in a short time in all cases and was followed by profound sleep. The patients were out of bed the next day and back to duty on the fourth day. Even the two patients in profound shock responded. No morphine was used, and antivenene was not available.

Sweet Potatoes (*Ipomoea batatas*)

By B. SEN

(Abstracted from the *Current Science*, Vol. 18, May 1949, p. 152)

IN India sweet potato is commonly looked upon as an inferior food crop. In spite of the fact that sweet potato can help in a great measure to relieve our acute shortage of both food and fodder, up to this time it has not attracted the attention it deserves.

Even in the U.S.A., the increased interest in sweet potato is of comparatively recent origin. It was the demand of the army for dehydrated food during World War II, and stoppage of normal imports from abroad of root starch, which brought out the importance of sweet potato in the U.S.A.

TABLE

Composition of food (edible portion in one pound)

	Calories	Protein	Fat	Carbohydrates	Calcium	Phosphorus	Iron	Vitamin A	Thiamine	Riboflavin	Niacin	Ascorbic acid
		gm.	gm.	gm.	gm.	mg.	mg.	units	mg.	mg.	mg.	mg.
Sweet potatoes	567	8	0.5	127	159	222	3.2	17,200	0.45	0.32	5.9	113
Irish potatoes	386	9	3.0	87	36	222	3.4	180	0.41	0.23	5.4	45

abdominal pain, often cramp-like as in an acute surgical condition of the abdomen; cramp-like pains in the legs, arms and back; a general feeling of "utter weakness"; restlessness and extreme fear reaction, often hysteria, headache, nausea and vomiting; and burning of the soles of the feet (in unknown types of bites this symptom may be pathognomonic).

'In children there may be convulsions which are extremely difficult to control. Other possible symptoms are variable such as paralysis, cyanosis, dyspnoea and urinary retention.'

Physical examination in this series revealed the following: The site of injection usually showed an area of erythema with mild oedema (in 2 cases the site was not evident); a board-like abdomen, non-tender to palpation, was present in all cases; there was hypersensitivity of the skin, the calf muscles were tender to palpation; 2 patients were in profound shock with blood pressure unobtainable (the other 4 patients

Dr. Julian C. Miller of Baton Rouge, Louisiana, has estimated the comparative nutritive values of edible portions of ordinary white potato and sweet potato. His unpublished data are produced in table.

It will be seen from the above table that sweet potato ranks higher than ordinary potato in most categories, particularly in carbohydrates, calcium and vitamin A. Moreover, the yield of sweet potato per acre has been found to be higher than that of ordinary potato. Tender end-lengths of sweet potato vines can also be used as a table spinach. A few plants would be sufficient to supply the spinach requirements of a family for a whole season. Small samples of sweet potatoes can easily be sun-dried by the cultivators and made into flour for their own use, as is now commonly done in villages in India where sweet potatoes are cultivated. For handling large quantities, modern dehydrating machines can be utilized with profit. Experimental trials in India have shown that 20 per

cent of sweet potato flour, or even more, can be mixed with atta for chapattis. The result is both nutritious and palatable.

Apart from the higher yield of the edible roots of sweet potato, as compared with ordinary potato, the vine terminals and leaves constitute an excellent source of fodder. Nearly 1½ tons of high quality dried sweet potato leaf meal can be obtained per acre. The feed value is approximately equal to that of alfalfa hay.

Thus the roots and tender vine end-lengths of sweet potato offer a very nutritious food for human beings, and the stringy roots and the bulk of the stems and leaves make an excellent fodder for cattle.

Sweet potato also has a number of important industrial uses: it can be utilized for the manufacture of starch, industrial alcohol, pectin, carotene and syrup.

Physiology of the Menopause

By S. L. ISRAEL

(Abstracted from the *American Practitioner*, Vol. 3, April 1949, p. 481)

THE primary alteration is probably in the ovary, which gradually fails to respond to stimulation from the pituitary. The absence, however, of the corpus luteum hormone, progesterin, results in endometrial changes and in the disappearance of pregnandiol from the urine.

The diminution or cessation of the production of estrogen by the ovaries is accompanied by remarkable changes in the anterior hypophysis. More recently, the studies of Severinghaus of the activity of the anterior hypophysis in post-menopausal women have demonstrated a high state of activity of both the basophiles and the acidophiles, activity which includes an increase in both the rate of elaboration and the release of their secretory products. There is an interesting sex difference in this regard inasmuch as the hypophysis of this senescent male does not possess the cytologic features of hyperactivity but shows rather every sign of retrogressing function.

The excessive gonadotrophin, frequently more than twenty times the average normal, may appear before menstruation ceases, and may persist for many years.

The uterus becomes smaller. The endometrium shows many patterns, depending on the character—ovulatory or anovulatory—of the terminal cycles and on the quantity of post-menopausal estrogen present. Deprived of these natural barriers to infection, the vagina becomes fertile soil for bacterial growth. The atrophy and subsequent infection give rise to the symptoms of irritating leukorrhœa, introital paræsthesia, and dyspareunia.

The shrinking of the genital organs includes the loss of muscular tone and fascial strength.

TREATMENT

It is an undeniable fact that every woman who passes through the climacteric undergoes physiologic changes. However, relatively few women suffer really disturbing symptoms because of them. The most important decision to make in the management of an ill woman during the climacteric is to decide whether or not her complaints are of menopausal origin. To be certain that no other illness, one unrelated to the menopause, is present, it is imperative that a thorough history be taken, a complete examination made, and the personality of the patient evaluated.

Most women passing through these eventful years do not require specific treatment for the menopausal syndrome. In this majority group, the flushes, headache, and nervous instability are mild, and may be

completely mitigated by consultation alone. An explanation of the temporary nature of the symptoms, and of their tendency to disappear spontaneously after a variable time coupled with the sympathetic prescription of a mild sedative, may be all that the patient requires. However, when the symptoms of menopause are really troublesome, there is no more specific therapy than estrogen.

Estrogen therapy.—The objective of therapy with estrogen is to minimize the intensity of the duration of distressing symptoms, as well as to tide the patient over the period of physiologic adjustment. The symptoms vanish in almost all instances if the estrogenic therapy is adequate and well planned.

The oral route of administration of estrogen is particularly suited to menopausal therapy. Most of the orally effective estrogens are efficacious in doses five or more times the hypodermic dose. With the availability of such potent oral preparations, there seems to be no need for parenteral administration of estrogen in the treatment of the menopausal syndrome. A positive advantage of oral therapy, with any of the estrogens, is the fact that a distinctly smoother control of symptoms may be obtained by the taking of one or more doses daily than by any of the ordinary injection procedures at intervals of a week or more. The smallest oral dose required to assuage vasomotor symptoms should be prescribed, and it should be prescribed according to definite rules. Whether one employs a daily dose of 0.625 mg. of estrone sulphate, 0.2 mg. of dienestrol, 0.5 mg. of stilbestrol, or 0.02 mg. of ethinyl estradiol is immaterial. The important precepts are to prescribe the estrogen for a limited period and to withdraw it in a gradual manner. The most prevalent abuse in the usage of estrogen is the prescription of a routine daily dose to be taken more or less indefinitely. This often eventuates, even in women who had long since ceased to menstruate, in the occurrence of uterine bleeding. Such bleeding also frequently follows sudden withdrawal of the estrogen. It must be emphasized that the objective of estrogen therapy of the menopausal syndrome is to aid the patient's adjustment to the diminution and cessation of ovarian function. This logical aim is lost if the estrogen is not prescribed for measured periods, with repeated attempts to withdraw the hormone entirely. When the latter is accomplished gradually, withdrawal bleeding is less likely to occur. It does, however, also occur in some of the properly controlled patients in whom the endometrium is peculiarly sensitive to estrogen.

Contra-indications to estrogen therapy.—Despite the fact that estrogen has definite value in the control of the menopausal syndrome, it cannot be universally applied. There are certain women in whom estrogen therapy is potentially dangerous. The administration of estrogen is ill advised under the following circumstances:

1. In the presence of pre-menopausal menstrual irregularity. Estrogen may result in even more irregular bleeding, thus confusing the diagnostic issue.

2. In a woman castrated because of endometriosis. It must be assumed that any patient who has undergone bilateral oophorectomy because of advanced and disseminated endometriosis still harbours foci of ectopic endometrium. If such residual are in a vital site such as the rectum, estrogen-evoked reactivation of the lesion may result in serious hæmorrhage.

3. In women of cancer families. Even though the clinical evidence of the alleged carcinogenic tendency of estrogen in the human female is quite indirect, it is safer to assume that estrogen, being a stimulant to growth of the genital organs and the breasts, may awaken a potentially malignant substratum. It is an obvious corollary that estrogen is also contra-indicated if the patient herself is a salvaged survival of either mammary or uterine neoplasia.

4. In the presence of uterine myomas and of mammary fibro-adenomas. Estrogen is a physiologic



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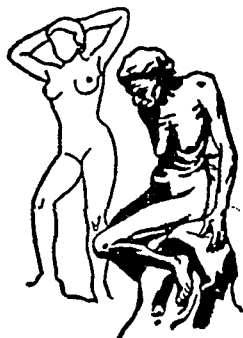
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trophic agent to the mammary ducts, as well as to the myometrium. As such, it should not be administered when there is a possibility of increasing the growth of tumours of those tissues.

5. In a patient with a history of recent hepatitis. The liver, through its alteration of circulating estrogen, plays a dominant rôle in determining how much biologically-free estrogen is available to effect changes in the estrogen simulated end-organs. It is conceivable that severe hepatitis may result in temporary hepatic decompensation in so far as estrogen metabolism is concerned, thus resulting in abnormal end-organ response to the excessive quantity of circulating estrogen.

Use of Anti-histaminic Drugs in Human Tuberculosis

JUDD AND HENDERSON report on the use of anti-histaminic drugs in 30 cases of human tuberculosis in which the clinical report was graded roentgenographically and by temperature changes. Character and quantity of sputum, increase in weight, appetite, and feeling of well-being were noted. The greatest improvement occurred in patients with tuberculous pneumonia and other acute exudative lesions which are a result of hypersensitivity. It is significant that, as the lesions progress in chronicity, the anti-histaminic drugs become less effective.

Mantoux tests were performed on all patients. Purified Protein Derivative Tuberculin, USP, was used

prior to, during, and after administration of the drug. In most instances, a gradual diminution in the intensity of the reactions occurred while anti-histaminic drugs were taken. The conversion was not always complete, however, and many individuals occasionally showed a slight positive reaction. The reaction became positive within about four to six weeks after administration of the anti-histaminic drug was stopped.

Although skin sensitivity is not necessarily a measure of hypersensitivity existing in other tissues, it would appear from our results that clinical improvement roughly parallels suppression of the Mantoux reaction. Three of the patients who showed striking improvement coincident with anti-histaminic therapy were taken off this medication. Within two to eight weeks, symptoms and signs of the disease recurred and retrogression of the pulmonary lesions were demonstrable by x-rays.

Reinstitution of therapy was again followed by striking improvement in all three patients. In these patients, the clinical improvement accompanying the administration of the anti-histamines strongly points to the therapeutic effectiveness of these drugs even though improvement lasted only through the administration. The combined administration of anti-histaminic drugs to suppress the allergic components of the disease, and streptomycin to suppress the growth of the bacillus, may be very effective treatment. Such combined therapy is under active investigation. Additional clinical investigation is in progress.

(Dr. A. R. Judd and Alfred R. Henderson: The Use of Anti-histaminic Drugs in Human Tuberculosis: A Preliminary Report. *Annals of Allergy*, 7, 306-317, May-June 1949. Dr. Judd is connected with the Pennsylvania State Department of Health, Hamburg, Pennsylvania.)

Reviews

A DESCRIPTIVE ATLAS OF RADIOGRAPHS.—By A. P. Bertwistle, M.B., Ch.B., F.R.C.S. (Edin.). Seventh Edition. 1949. Henry Kimpton, London. Pp. xxx plus 622, with 980 illustrations. Price, 50s.

'A DESCRIPTIVE ATLAS OF RADIOGRAPHS' first appeared in 1926 to stimulate interest among students and practitioners in the vast possibilities of x-rays in medical diagnosis. 'Written by a clinician for clinicians', it is admirably suited for this purpose, covering a greater part of the subject.

It is felt, also, that the substitution of negative skiagrams in place of positives and 'the silhouette radiograph' should greatly enhance the value of the book, as many of the present reproductions leave a lot to the imagination.

A very pleasing and stimulating feature of the book is the comprehensive and detailed section of the history of medical radiodiagnosis. All medical men, radiologists in particular, will find in 'Milestones in Radiodiagnosis' much to interest them and to bring home the fact that this branch of medicine is but fifty years old—fifty years of intense progress and advance.

J. A. S.

NOTES ON INFANT FEEDING.—By G. B. Fleming, B.A., M.D., F.R.C.P. (Lond.), F.R.F.P.S., and Stanley Graham, M.D., F.R.C.P. (Edin.), F.R.F.P.S. Third Edition. 1948. E. and S. Livingstone Limited, Edinburgh. Pp. 66. Price, 3s.

THESE notes primarily compiled for medical students embody the principles of infant feeding which are followed at the Royal Hospital for Sick Children, Yorkhill (Glasgow). The subject has been consider-

ably simplified but fundamentally based on physiological considerations. The booklet contains instructions for feeding of both normal and sick infants as regards the quantity as well as the quality of the diet and at the same time simple enough for the mother to carry out. There is an appendix containing useful informations.

R. N. C.

'BED-SIDE MEDICINE'. A TEXTBOOK OF MEDICINE, CLINICAL AND SYSTEMATIC, WITH ETIOLOGY, PATHOLOGY, SYMPTOMATOLOGY, PHYSICAL SIGNS, TREATMENT AND LABORATORY METHOD, WITH SPECIAL REFERENCE TO DISEASES COMMON IN INDIA.—By Ral Akhil Ranjan Majumdar Bahadur and Susil Chandra Chatterjee. Eighth Edition. Scientific Publications Concern, Wellington Square, Calcutta 13. Pp. 1324 plus xl. Price, Rs. 22

MAJUMDAR'S 'Bed-Side Medicine' is well known. In this edition the book has been thoroughly revised and in many places rearranged and rewritten, incorporating recent advances. It has now grown in size by over 200 pages and nearly 200 new diagrams have been added. The authors appear to have devoted considerable labour in making the book useful to students for whom mainly it has been designed.

R. N. C.

THE SEPTENNIAL (1939-1946). REPORT OF THE DEPARTMENT OF RESEARCH, UNIVERSITY OF TRAVANCORE, TRIVANDRUM. 1948. Pp. 594

THIS report is the first of its kind and is intended to serve not only as a register of work done but also as a basis on which the future development of the State activities may be planned.

curds with our rice or in a diluted form as 'Maththa', 'Lassi' or 'Chaas' as a drink or during our meals, we consume not only lactic acid organisms but also 'Torula dahi', which produces vitamin B complex and p-amino-benzoic acid, etc.

In view of the above information the possibility suggests itself that sulpha drugs might prove ineffective in the case of patients to whom these drugs are administered, if they happen to take a diet in which curds or other preparations of curds are included.

We wonder if any such effect has been observed in making the action of sulpha drugs, for instance, ineffective because of the patients consuming curds or 'dahi' and if so whether the physicians would consider the desirability of stopping curds in any form to the patients who are under treatment of sulpha drugs.

N. V. JOSHI.

BIOCHEMICAL AND MICRO-
BIOLOGICAL LABORATORIES,
FERGUSON COLLEGE,
POONA 4.

MEDICAL POST-GRADUATE COURSES

SIR,—The Special Educational Number of May 1949 of the *Indian Medical Gazette* has just arrived in U.K. and I read it on the 16th September, 1949, in the Faculty Library of the Physicians and Surgeons of Glasgow.

I liked the editorial very much. It is interesting in view of the visit of the Health Minister of Great Britain, Mr. Aneurin Bevan, to our country for planning the National Health of Bharat (India). The special article from the pen of a veteran like Dr. U. B. Narayanrao of Bombay has a special value of its own.

I agree with 'graduate, F.R.C.P.' in allowing medical men to come to U.K. and U.S.A. until we can start our post-graduate medical institutions in India to train people in special subjects like Dermatology, Venereology, Orthopaedics, Cardiology and the like. According to Bhoré Committee every medical college must have every special branch of medicine and surgery under specialists.

The letter of Dr. P. R. Dasgupta of Simla is important and it is high time that the Indian Medical Association or the Director of Medical and Health Services, India, should start post-graduate medical institutions in India. The Calcutta School of Tropical Medicine is no way inferior to any of the post-graduate institutions in this country and post-graduate teaching is done also in tropical medicine there. Then why not convert this Calcutta Tropical School into the first post-graduate medical institution? Keeping the name and everything unchanged only arrangements may be made for teaching of different subjects and advantage of so many first-class hospitals can be taken for clinical teaching of the special subject. Further the Licentiates L.M.F., L.M.P., L.C.P.S. should have two years' post-graduate training with lectures in the Calcutta School of Tropical Medicine in Medicine, Surgery, Ophthalmology and Obstetric Medicine and after proper examination should get M.I.T.M., that is Member of the Institution of Tropical Medicine (Calcutta). Any one having M.B., B.S. and M.I.T.M. can be eligible for F.I.T.M. (Fellow of the Institute of Tropical Medicine), if he has worked for seven years in the special department and at the same time attended the special course of training (Lectures and Clinics) for one year of the Calcutta School of Tropical Medicine. The specialist may be styled as F.I.T.M. (Cardiology), F.I.T.M. (Dermatology), F.I.T.M. (Ophthalmology), F.I.T.M. (Paediatrics), F.I.T.M. (Surgery), F.I.T.M. (Eye or ENT), etc.

The Glasgow F.R.F.P.S. wants a candidate to have worked in a responsible post in the special department for a period of 7 years to sit at the F.R.F.P.S. Examination.

The lectures can be arranged as are arranged in London, Edinburgh and Glasgow, for the different post-graduate courses and lecture theatres of different hospitals and colleges can be utilized as well as the staff of the five different medical colleges as well as of two post-graduate medical institutions of Calcutta. A start should be made without much delay.

The post-graduate classes should start next year and should be advertised for such courses right from now in all the provincial medical journals as well as in the Journal of I.M.A. and notices should be sent to different medical colleges of all the provinces in India. M.D., M.S., M.C., D.G.O., D.O.M.S., D.C.H. of Indian universities will be there but M.I.T.M. will bring the licentiates to the same levels as the M.R.C.P. (Edinburgh, London or Ireland) does to the conjoint or triple qualification holder in this country. F.I.T.M. will certainly be a higher post-graduate qualification and will be equivalent to F.R.C.S. (England, Edinburgh, Ireland or Glasgow) and M.R.C.P. (Edinburgh, London or Dublin) or F.R.F.P.S. (Glasgow). But the standard should be very high and the examination should be equally stiff.

Yours faithfully,

(Sd.) K. D. LAHIRI,

Clinical Assistant in Dermatology,
Glasgow University and Hospitals.

Dated 16th September, 1949.

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

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Original Articles

NEUROMYELITIS OPTICA (DEVIC'S DISEASE)

A CASE REPORT

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A HINDU girl, 4 years old, had fever with rigors $1\frac{1}{2}$ years back. This fever lasted for $1\frac{1}{2}$ months, during which period there was gradual paralysis of the lower extremities (figure 1, plate XXXI), affection of the sphincters, vomiting, drowsiness and occasionally convulsions. A month after the onset of the paraplegia, the parents found that the vision began to diminish. The child was completely blind in 4 months. Previous to this the child had not suffered from any exanthematous fever or acute infections. There was no history of syphilis in the parents. The child herself had no stigmata of congenital syphilis. It is to be surmised that the optic nerves must have been attacked fairly early in the disease, and the parents became aware of the dimness of vision when it became gross.

She was treated at various clinics, without any benefit. During this period she was given a lot of vitamin B₁. I saw this case on 10th February, 1948, it being referred to me by two of my friends, one a general surgeon, and the other a consulting physician. I confirmed the diagnosis of neuromyelitis optica, which the physician had made. The patient on fundoscopic examination had chalky white discs, without any other changes in the surrounding fields. The pupils were immobile and dilated. The paraplegia with exaggerated reflexes still persisted.

As large amounts of vitamin B₁, given orally and parenterally, were ineffective, I injected vitamin B₁ intrathecally, starting with 15 mg. and repeating it every 5 days. There was improvement after the second injection; the child tried to get up. After the third injection on 12th March, 1948, she attempted to squat, the incontinence disappeared and the vision improved in the left eye, sufficient to perceive light and hand movements, though there were no changes in the discs (figure 2, plate XXXI). She then developed chicken pox during the course of treatment, which had to be temporarily stopped. The 4th injection of 25 mg. was given three weeks later (8th April, 1948). Then she was able to see objects and to walk with support. The right eye was still blind. I might here mention that vitamin B₁ was given orally in

doses of 20 mg. three times a day during the period the child was laid up with chicken pox.

Thirty and 35 mg. were injected on the 22nd April and 6th May respectively. She could then walk without support though with faulty gait, and slightly bent forwards. She could see much better. After another injection of 45 mg., she was able to get about without support and was even able to run. On the 18th of June she was able to see moving bodies with the right eye also. The dose was then raised to 50 mg. and the injection thereafter was given at an interval of a month. Ultimately on 15th July, after the last injection of 60 mg., the child was asked to have no more treatment for some time. By this time she was able to walk properly and see with both eyes, though the vision in the left eye was better than in the right.

Unfortunately and unexpectedly, the child died suddenly on 6th October, 1948, with no premonitory symptoms. According to her father the night before her death, the child ate well and slept well. On the next morning she was up and playing. She was being brought to the hospital, and when the father was about halfway from his village, the child suddenly had a seizure and died on the spot. She had complained at breakfast that morning of some pain in the abdomen. There was no fever according to the father's history of the incident. One can only imagine the cause of the unfortunate child's end, who at first escaped right from the jaws of death to succumb to it a little later.

Neuromyelitis optica is a rare disease and up to date only 130 cases have been reported in the literature. Allbutt in 1870 noted a definite relation between a bilateral optic neuritis and a myelitis. In 1879, Erb noted the same phenomenon. It was however left to Devic in 1894 to definitely confirm it as a clinical entity, and since then it has come to be known by his name.

This is a demyelinating disease of the central nervous system and can actually be said to be one of the four clinical types, viz: (1) Disseminated sclerosis, (2) acute disseminated encephalomyelitis, (3) neuromyelitis optica, and (4) encephalitis periaxialis diffusa of Schilder. The ætiology of these diseases is uncertain and, as Paton (1936) describes them, they are four virus infections with the nature of the causative factor obscure, a virus unknown at present. He attributes the difference in the four types either to a variation in the virulence of the toxin, or to the difference in the existing susceptibility of the affected structures.

However, all four have one main common characteristic, and that is the early involvement of the optic nerves, the myelin sheath of which is attacked foremost, or simultaneously with that of the spinal cord tracts, or of the centrum ovale. Berliner (1935) thinks it possible that all the four types are variations of one main entity.

Nevertheless, it is universally acknowledged now that the most likely hypothesis is that a neurotropic virus is responsible for the production of these conditions.

Pathology

There are acute inflammatory lesions, with demyelination and perivascular infiltration. The destroyed myelin substance is absorbed by the microglial phagocytes. The axis cylinders degenerate and proliferative gliosis is the final sequence. The neuritis is characteristically retrobulbar, since the nerve fibres which are myelinated are attacked. The myelitis in some 50 per cent of cases proves fatal due to the ascending involvement of vital centres in the medulla. In neuromyelitis optica as in acute encephalomyelitis, the incidence of bilateral and extensive involvement is greater and remission is a rarity.

Thus Devic's disease is an acute infection, without any demonstrable definite causative factor. The symptoms presented are those of ascending myelitis and bilateral optic neuritis which are simultaneous. Other characteristics are that there is no specific age group, the course of the disease is rapid and more often than not is fatal. The laboratory, serological and urinalysis findings are negative.

Since thiamin chloride remains in the cerebrospinal fluid for a longer time when injected into and mixed thoroughly with the C.S.F. and since it is excreted very slowly, if given by this route, it is rational to believe that it would exert a definitely beneficial effect on the central nervous system. Again since experimental avitaminosis B₁ reveals marked myelin degeneration in the spinal cord as well as in the peripheral nerves (Gildea *et al.*, 1936), it is logical to believe that intrathecal vitamin B₁ therapy should be the one of choice. Stern (1938) reports very favourable results in his 2 cases of multiple sclerosis treated by the intrathecal route. The patient described and treated by me received 10 intrathecal injections between 2nd March, 1948, and 15th July, 1948. The maximum dose given was 60 mg. According to Stern (1938), 100 mg. of vitamin B₁ injected intrathecally might prove fatal. So it is dangerous to exceed this dose, or even to approach very near this limit.

Now of course to be honest, whether it is the vitamin B₁ given intrathecally or whether it is the normal course* of the disease, that has given such spectacular results, who can tell? Coincidence of treatment with natural improvement* is a very misleading and disconcerting factor in the assessment of the therapeutic value of different remedies.

* Remission is not a feature of this disease according to Wachsler, W. E., 1947. A Textbook of Clinical Neurology, W. B. Saunders Co.—Editor, I.M.G.

Summary

A rare case of a rare disease neuromyelitis optica is reported, wherein the patient was affected with the disease, and received continuous treatment for one year without any benefit. Thereafter, 10 injections of vitamin B₁ in increasing doses and at certain intervals were given intrathecally to the patient who responded well to this treatment apparently, and ultimately recovered her vision to some extent as well as recovered from the paraplegia. The sudden death, full 3 months after the last dose, is inexplicable since the patient was not seen after the death, nor was post-mortem examination possible. The perimetric examination of the patient's field of vision was not possible due to her age.

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THE TREATMENT OF FEMALE GENITAL DISORDERS WITH STEROID HORMONES

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A report on 700 cases

It is my object in the present article to give an account of a few of the various female genital disorders and the treatment adopted by me with hormones during the last 12 years.

(A) Treatment with female hormones

The rationale of oestrogen therapy is based upon certain physiological considerations. The female hormones produced by the ovaries are oestrin and progesterone. While the former is secreted continuously from almost the very beginning of life, in the mature female its effects are responsible for the maintenance of such secondary sex characteristics as the shape of the female breasts, the size of the adult uterus and adnexa, and the 'oestrus' condition of the vaginal mucosa. Progesterone, on the other hand, is secreted in the menstrual cycle only for a few days every month.

The physiological actions of the two hormones are entirely different. Oestrin is essential for the development of the sex organs and determines femininity, and its absence will prevent ovulation and consequently there will be no menstruation. It sensitizes the uterus and increases its vascularity and motility while progesterone desensitizes

it and inhibits its motility thus allowing the nidation of the ovum and preventing the occurrence of abortion. Both hormones are necessary for menstruation and pregnancy to occur.

Deficiency of those hormones brings about the various disorders which have to be treated by supplying the body with an adequate amount of them to make good the shortage and thus correct the various abnormalities that occur as a result.

Endocrine therapy in the human female has undergone considerable changes in the past few years and of practical value in the management of clinical endocrine problems in women are the two synthetic female hormones oestradiol and progesterone. These preparations have been used during my practice abroad and in this country for twelve years, and the results obtained in their varied applications are given below. The treatment was carried out in the following main disturbances:

- (1) Hypogonadism, hypoplasia and infantilism.
- (2) Primary amenorrhœa.
- (3) Hypomenorrhœa.
- (4) Disturbances and deficiencies during the climacteric.
- (5) Eczema.
- (6) Metropathia hæmorrhagica.
- (7) Habitual abortion.
- (8) Threatened abortion.

Case reports

(1) *Hypogonadism, hypoplasia and infantilism* (combined with dysmenorrhœa and sterility).—Average age of the patients 18 to 20 years; married, coitus painful. The internal examination showed a small uterus, not completely developed and the examination was painful.

Average periodical cycle 5 to 7 weeks, scanty flow oligomenorrhœa.

Treatment.—Five injections of oestradiol dipropionate, 1 mg. each, were given with an interval of 3 to 4 days, starting with the cessation of the last period. The course of the treatment was 2 to 3 months. Most of the patients had their regular periods after the 2nd course but to be on the safe side a 3rd course was also given. The final examination after the full course of treatment revealed a normal development of the uterus; no pains during examination of coitus were felt. The vaginal secretion was present and in several cases conception was seen after the treatment.

Number of cases treated: 308.

(2) *Primary amenorrhœa.*—The age of the patients was 16 years and over. Some of them were virgins, though married, on account of fear of pain during tried cohabitation. They were brought by their husbands. In most cases the patients were infantile, frightened and

eagerly awaiting the result of the examination, which in nearly all cases showed a small undeveloped uterus, about the size of a big walnut, mostly retroverted, hard and dried up. There was no libido. The vagina was dry, the hair on the mons veneris scarce, the breasts were small and undeveloped and the hips of a masculine type. These patients never menstruated.

Treatment.—Four injections of 5 mg. each of oestradiol dipropionate were given intramuscularly into the buttocks with intervals of 5 days (in some cases in combination with anterior pituitary hormone, daily 1 cc.). Six days after the last injection of oestradiol dipropionate the treatment was continued by 3 injections of progesterone, 5 mg., every second day to complete the cycle. The same course of treatment with oestradiol dipropionate and progesterone was repeated during 2 or 3 cycles. Within this period the uterus and pubic hair developed normally; the breasts and buttocks showed a more feminine shape; nervousness and fear of cohabitation disappeared in about 95 per cent of the cases. The patients became more self-confident. A normal menstruation was experienced for the first time, and continued regularly every month.

Number of cases treated: 150.

(3) *Hypomenorrhœa (primary).*—In all these cases a regular but scanty flow of menstruation was observed.

Treatment.—After the cessation of the last menstruation the following treatment was given:

First day 1 mg. oestradiol dipropionate intramuscularly; 2nd, 3rd and 4th days 1 mg. oestradiol orally per day; on the 5th day 1 mg. oestradiol dipropionate intramuscularly; on the 6th, 7th and 8th days 1 mg. oestradiol per os and so on until the 21st day ending with an injection. Three days before the expected period, one tablet of anhydrohydroxyprogesterone 5 mg. was given and this dosage was continued during the first two days of the menses. The menses became normal after 3 to 4 cycles of the above treatment. To be on the safe side this was continued for 3 months by oral administration of 15 oestradiol tablets of 1 mg. during the first 15 days of the intermenstruum and 5 tablets of anhydrohydroxyprogesterone during the last 3 days of the intermenstruum and the first 2 days of the menses (and so on). All cases of hypomenorrhœa were treated successfully.

Number of cases treated: 79.

(4) *Disturbances and deficiencies during the climacteric*, such as senile vaginitis, pruritus and kraurosis vulvæ, loss of pubic hair, arthroses, psychic depressions, flushings, etc.

Treatment.—One mg. of oestradiol dipropionate intramuscularly every 3rd to 4th day and local applications of oestradiol ointment were given until the symptoms vanished. 93 per cent of these cases were treated successfully.

Number of cases treated : 30.

(5) *Eczema*.—For the treatment of feminine eczema during the menopause oestradiol ointment was used with great success. Successfully treated : 83 per cent of the cases.

Number of cases treated : 36.

(6) *Metropathia hæmorrhagica*.—Ten mg of progesterone were given intramuscularly every day until the bleeding stopped. Duration of this treatment : 10 to 20 days. After an interval of a week to a fortnight the injections were repeated a few days before the expected menstruation. This treatment was discontinued only when the period was normal. After the menses had become normal a supplementary course of 1 tablet of 5 mg. anhydrohydroxyprogesterone per day was given (5 days before the commencement of each menstruation) and was continued for 6 months. The results were satisfactory in all cases.

Number of cases treated : 12.

(7) *Habitual abortion*.—In cases of habitual abortions, as soon as pregnancy was diagnosed, the following treatment was given :

Five mg. of progesterone were injected intramuscularly every second day. Then the dosage was gradually reduced to 2 mg. every 3rd or 4th day. During the days corresponding with the past menstruations 5 mg. a day were given by injection. From the beginning to the end of the pregnancy 1 tablet of 50 mg. vitamin E per day was given. This treatment proved successful in 80 per cent of the cases.

Number of cases treated : 15.

(8) *Threatened abortion*.—Some of the pregnant women came after the first signs of bleeding, some, however, only after 2 or 3 days of bleeding. In all cases 10 mg. of progesterone were given intramuscularly every day until the symptoms ceased. The dosage was then reduced slowly to 5 mg. and the interval increased to 2, 3 and 4 days. Finally, the treatment was continued by the oral administration of 5 mg. of anhydrohydroxyprogesterone per day. Vitamin E was given in all these cases for at least 3 months. The administration of anhydrohydroxyprogesterone was discontinued 6 weeks after the first signs of threatened abortion. The usual methods of treating threatened abortions were applied, i.e. rest in bed with the foot-end of the bed raised as against the head-end. In 3 cases the bleeding re-occurred. In these cases the treatment was repeated with 10 mg. of progesterone intramuscularly until the cessation of bleeding. 77 per cent of the cases were treated successfully.

Number of cases treated : 25.

(B) *Treatment with male hormones*

In the treatment of premenstrual pain in the mammae, testosterone propionate was given with great success. In most cases one injection of 10 mg. intramuscularly was fully successful. In cases, however, where the pain was not relieved by this treatment, 3 injections of 10 mg. of testosterone propionate on successive days were given. The treatment was successful in 100 per cent of the cases.

Number of cases treated during the last 16 months : 45.

TABLE

Indications	Number of cases	Treatment	Number of cases treated successfully	Percentage of successfully treated cases
Hypogonadism, hypoplasia and infantilism.	308	Oestradiol dipropionate	308	100
Primary amenorrhœa ..	150	Oestradiol dipropionate and progesterone, in a few cases in combination with the anterior pituitary hormone.	142	95
Hypomenorrhœa	79	Oestradiol dipropionate, oestradiol and anhydrohydroxyprogesterone tablets.	79	100
Disturbances and deficiencies during the climacteric.	30	Oestradiol dipropionate and oestradiol ointment.	28	93
Eczema	36	Oestradiol ointment	30	83
Metropathia hæmorrhagica ..	12	Progesterone and anhydrohydroxyprogesterone tablets.	12	100
Habitual abortion ..	15	Progesterone. Vitamin E was administered additionally.	12	80
Threatened abortion ..	25	Progesterone and anhydrohydroxyprogesterone tablets. Vitamin E was administered additionally.	19	76
Premenstrual pains in the mammae.	45	Testosterone propionate	45	100
TOTAL NUMBER OF CASES ..	700		675	96.4

Summary

During the last 12 years notes were made on 700 cases of female genital disorders, such as hypogonadism, hypoplasia, infantilism, primary amenorrhœa, hypomenorrhœa, disturbances and deficiencies during the climacteric, eczema, metropathia hæmorrhagica, habitual abortion and threatened abortion. In 675 of these cases, i.e. 96.4 per cent were treated successfully with oestradiol dipropionate, oestradiol progesterone, anhydrohydroxyprogesterone or a combination of the above-mentioned ovarian and corpus luteum hormones, and some cases with testosterone propionate. In habitual abortion vitamin E was administered in addition to treatment with progesterone. In threatened abortion the treatment with progesterone and anhydrohydroxyprogesterone was also combined with vitamin E per os. In primary amenorrhœa, the anterior pituitary hormone was given in some cases in addition to the above oestrogenic and luteal hormones.

The results of the treatment with steroid hormones given in the table and showing a success in 96.4 per cent of the cases are very encouraging indeed. No adverse by-effects on account of the above treatment were ever seen during all these 12 years.

The preparations used in the above study were: oestradiol dipropionate 'Ciba' (ovocyclin P); oestradiol 'Ciba' (ovocyclin); progesterone 'Ciba' (lutocyclin ampoules); anhydrohydroxyprogesterone 'Ciba' (lutocyclin tablets); and testosterone propionate 'Ciba' (perandren).

PROGESTERONE IN THE TREATMENT OF MALARIA

By S. J. GROSS, M.D.

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I SUGGESTED in a previous communication (Gross, 1947) that sex hormones participate in the mechanism of malaria. Abortions, sterility, impotence, menstrual disorders, greater susceptibility of women to malaria, predominance of female parasites in the blood, and recurrences of malaria at regular intervals of 3 to 4 weeks are manifestations and sequelæ of malaria which strongly suggest the participation of female hormones in the pathogenesis of malaria.

My original observations were made on men. In the meantime I have observed a number of malarial attacks in women. It is interesting that most of the women had the first attack of fever generally 2 to 3 days before menstruation or the expected date of their periods. I have observed this onset of malarial fever, first attacks and not relapses, shortly before menstruation so often and so regularly that I am

inclined to regard fever 2 to 3 days before menstruation as a diagnostic sign for malaria.

Shortly before menstruation the secretion of progesterone decreases and the secretion of oestrogen begins, both hormones being at a low level with follicular hormone in the ascendancy. A similar, though reversed, condition is encountered shortly before ovulation when the secretion of oestrogen decreases and the secretion of corpus luteum hormone increases. Putnam, Boyd and Mead (1947) reported periodic or cyclically recurring phenomena of vivax malaria in which a 12 to 13 days' rhythm or recrudescence is described. The authors have no explanation to account for it, except unknown aspects of the schizogonous cycle of the parasite. I believe that these cyclical recurrences can be explained by the normally occurring rhythmical changes in the hormonal level which enhance the onset of malarial attacks and of malarial relapses.

The known antimalarial drugs are excellent for the treatment of the acute malarial attack. However, they do not eradicate the infection and do not prevent the onset of relapses. Monk (1948) in a review of modern therapy of benign tertian malaria tabulates the results of 28 investigations with different drugs and different methods. From this table the average of the relapse rates is found to be 33.87 per cent. This indicates clearly that parasitocidal therapy alone is not sufficient. I have obtained and reported good results in the prevention of relapses with the administration of male hormones. It has been objected that male hormones might cause virilism when given to women patients (Deshmukh, 1947). This objection cannot be entertained, because in these cases testosterone propionate is given against an alleged excess of female hormones, and the dosage used and suggested is too small to cause any virilism. However, when given in the acute stage of the attack, these hormonal injections caused not too infrequently a rise of temperature. This rise does not occur when the injections are given in the convalescent stage.

Therefore I was looking for some hormonal preparation which could be given in the acute stage without causing any rise of fever. Corpus luteum hormone is the natural and logical choice. Follicular hormone is counteracted not only by the male hormones but to a certain extent also by progesterone. Corpus luteum hormone resembles the male hormone in some of its effects. This bi-sexual character of progesterone may be related to the fact that chemically it resembles much more the male than the female hormone. Progesterone is found in the adrenal cortex and it has been shown conclusively that the lives of adrenalectomized rats, ferrets and dogs will be prolonged by progesterone (Anderson and Bolin, 1940). In this connection it may be recalled that 'the implication of the adrenal gland is held to be responsible for algid malaria symptoms observed

during life, and that there is partial or complete loss of the yellow colour (lipoids) of the cortex and congestion and blockage of vessels with parasites' (Manson-Bahr, 1945).

In the present investigation I gave progesterone together with either quinine or mepacrine. Adults were given one injection of 2 mg. of corpus luteum extract for 2 to 5 consecutive days, according to the seriousness of the infection. Children were given a proportionately smaller amount. In serious cases progesterone was mixed with quinine in one syringe and given as single injection. The injections were usually followed by a fall of the temperature, and only in 2 out of 34 cases were these injections followed by a rise of temperature. These injections were given to men, women and children with uniformly good results. A few cases are described in the following :—

(1) B. V., Hindu male, 35 years old, gave a history of 10 days' fever at home. On admission to hospital B.T. rings were found. He was given quinine injections and mepacrine tablets without any noticeable effect. On the 4th, 5th and 6th day in hospital the patient was given injections of progesterone. The temperature came down and remained normal.

(2) S. R., a boy of 10 years, had fever for a few days prior to admission. In hospital he was given several injections of quinine and mepacrine tablets. This did not influence the temperature which varied between 102° and normal. After an injection of 1½ mg. progesterone the temperature became normal for 3 days. The patient had then another rise to 103°, but became normal after a further injection of corpus luteum extract. Thereafter the fever did not recur.

(3) Mrs. V., 25 years old, 7 months' pregnant, was admitted with fever of 4 days' duration. B.T. rings were found in the blood. Soon after admission to hospital she delivered a stillborn baby. The fever subsided only after 2 injections of progesterone had been given in addition to the routine malarial treatment.

(4) Mrs. V. P., 28 years old, had an abortion a fortnight prior to admission. The patient had a temperature of 103° and was given penicillin and sulpha drugs, as the fever was thought to be due to puerperal sepsis. The patient did not respond to this treatment, and on further examination *Plasmodium vivax* was found in the blood. With mepacrine and progesterone the fever came down promptly.

(5) Mr. D., 52 years old, suffered for years from chronic malaria. For the last three months prior to admission he had an attack of malaria every month. He came into the hospital with a further relapse which did not respond well to mepacrine and quinine. He was then given 2 injections of progesterone to which he responded immediately. It has to be mentioned that this patient was re-admitted to hospital with another attack or relapse after 11 months, and that

during the intervening period he had not had any attack whatsoever.

(6) Mr. B. B., a student, aged 22 years, had an attack of tropical eosinophilia six months prior to the present attack of malaria. On admission to hospital B.T. rings were found. He was given mepacrine and several injections of quinine combined with progesterone. However, the fever persisted. On further examination wheezing sounds and râles were heard over the right lung. A differential count showed now 16 per cent eosinophils. He was therefore given a few injections of acetylarsan, and the temperature came down to normal after the third injection. This case is interesting, because in this instance the attack of malaria apparently precipitated a relapse of eosinophilia and the condition did not respond to the specific anti-malarial therapy, but to arsenicals.

(7) The following case is of special interest : Mr. C. R., Hindu, 43 years old, had an attack of malaria two months ago. He came to see me with a chill which had begun 6 hours previously. He was given an injection of quinine 10 gr. to which 2 mg. of progesterone were added in the same syringe. The chill stopped 20 minutes after the injection, and the patient left without taking any further anti-malarial treatment. One month later he returned with a chill which had started 3 hours previously. Once more he was given the same injection with the same dramatic result. The result in this case is the more surprising, because quinine does not prevent the onset of malaria, and progesterone being in an oily solution could not act so quickly. It seems possible that progesterone and quinine might have a synergistic action and that due to this effect the manifestations were suppressed immediately. It has also to be considered that males react better to quinine than female patients.

I have used corpus luteum extract in combination with quinine or mepacrine for more than eight months. Thirty-four patients have been treated with this method. There was only one patient who, to my knowledge, has had a relapse. In my experience progesterone was of definite value in the treatment of malaria. In most, and especially in resistant and serious cases, the combination of progesterone and of quinine helped to bring the fever down. Nausea, vomiting, headache, pains in the joints, especially the pains in the lumbar area, subsided quickly after the injection of corpus luteum extract. Incidentally it might be mentioned that the same symptoms, when occurring during pregnancy, are also favourably influenced by progesterone. It seems possible that the pains in the lumbar area, so frequently encountered in malaria, are expressions of involvement of the sexual glands, as affections of these glands very often cause pains radiating to the lumbar area. Progesterone helped to shorten the duration of the fever attacks, and it had also a tonic effect. After

cessation of the fever the patients did not feel much exhausted, and progesterone contributed thus to a shortened convalescence.

Comment.—In many infectious diseases the destruction of the parasites represents only one phase of the defence process. In the second phase there is the development and increase of the natural resistance, a process which might be rather hindered than promoted by parasitocidal therapy alone. The biological defence can be stimulated and increased through administration of sex hormones. For instance, Anderson and Bolin (1940) have reported enhancement of resistance to administration of mouse-hamster strain of poliomyelitis virus by progesterone (complete protection), stilboestrol (mortality reduced from 68 per cent to 2.5 per cent) and testosterone (mortality reduced from 68 per cent to 20 per cent), while desoxycorticosterone failed to modify mortality. On the other hand, Bennison and Coatney (1948) investigating the sex of the host as a factor in *Plasmodium gallinaccum* infections in young chicks, found that female chicks showed higher parasite counts and earlier endothelial infections, and were less effectively protected by quinine. These investigations help to explain the beneficial action of progesterone in malaria, especially when given in combination with quinine, as demonstrated in case 7.

The relapses in malaria were suspected to be connected with the extra-erythrocytic cycle. Recent observations of Shortt and Garnham (1948) and Shortt *et al.* (1948) have thrown light on the pre-erythrocytic stage. These authors found the parasites in the liver on the 6th and 7th day, and they believe that the parasites are originally contained in the parenchyma of the liver. They conclude that 'the majority of the forms in the liver are nearly mature and at the stage immediately preceding merozoite formation'.

In another publication, Shortt and Garnham (1948) present evidence that the exo-erythrocytic cycle persists even after the establishment of blood infection, and they suggest that there might be a repetition of the intrahepatic process of exo-erythrocytic schizogony which is responsible for new relapses. These observations demonstrate the involvement of the liver. One of the functions of the liver is the inactivation of the oestrogens. Disease of the liver will interfere with the inactivation of the follicular hormones. Subsequently there will be an excess of oestrogens in the liver and in the organism. This excess of female hormones will favour the maturation of the pre-erythrocytic forms and of the merozoites in the liver which 'are nearly mature and at the stage preceding merozoite formation'. It can be assumed that the oestrogens will favour the maturation of these forms in the liver, as 'Oestrin is present in unicellular organisms and in young bacterial cultures in which it evidently acts as a general

growth hormone' (Cameron, 1940). This suggests the possibility that an excess of oestrogens which may result from various causes will enhance the maturation of those parasites which remained in the liver and in the organism after an attack. The oestrogens might thus contribute to the precipitation of a relapse. An excess of oestrogens might also increase the number of mature parasites and thus contribute to the seriousness of the infection. It has also to be considered that Korenchevsky and Ross (1940), investigating the effect of sex hormones on kidney, liver and heart, found that the oestrogens produce rather degenerative changes in these organs. An excess of follicular hormones might thus reduce the resistance of the affected, and allow the spread and multiplication of the parasites.

It is concluded that sex hormone therapy, progesterone in the acute and testosterone propionate in the convalescent stage, is beneficial in the treatment of malaria. This therapy counteracts an alleged excess of female hormones, increases the biological defence powers of the affected, and has a tonic effect. The hormones support and potentiate the action of the known antimalarial drugs.

Summary

Clinical facts indicate that there might be an excess of oestrogens concerned in the pathogenesis of malaria. This excess can be counteracted by progesterone. Progesterone resembles the male hormone and influences the adrenal gland which is involved in serious cases of malaria. Therefore corpus luteum extract has been used together with quinine or mepacrine in the treatment of acute attacks. Thirty-four cases have been treated with this method, and there was one relapse in this series. It is concluded that progesterone is of definite value in the treatment of malaria.

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THE PRECURSOR OF ASCORBIC ACID IN VITRO

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It seems conceivable that ascorbic acid may be produced by transformation of sugars or sugar acids of related structures, such as glycuronic acid or galacturonic acid or by total synthesis (Muslin *et al.*, 1939). The precursor of ascorbic acid is not probably of endogenous origin and is independent of carbohydrate intake (Mentzer and Urbain, 1938). Among many sugars investigated, mannose caused a greater rise of ascorbic acid than any other sugar (Guha and Ghosh, 1934). These findings, however, could not be confirmed (Scheumert and Schieblich, 1937; Hawthorne and Harrison, 1937). The presence of traces of manganese is necessary for the successful synthesis of ascorbic acid from mannose and to a less extent from galactose and glucose in animal tissues (Rudra, 1938).

The present investigation was undertaken in view of the certain discrepancies reported in the literature with regard to the synthesis of ascorbic acid by tissue slices with reference to the substrates from which ascorbic acid might be synthesized and the nature of its precursors. Attempts were also made to find whether magnesium in place of manganese was effective in giving better synthesis of ascorbic acid in presence of various hexose sugars.

Experimental

In the majority of the experiments adult albino rats were used. They were killed by stunning, and the various organs to be tested (liver, kidney, spleen, small intestines, etc.), were quickly removed and sliced. The slices were not washed, as washing removes an appreciable quantity of ascorbic acid. Nearly 0.5 g. of slices (weight depending on the number of slices to be made), weighed into a number of 2 oz. narrow-mouthed bottles were added to a mixture of 3 ml. Ringer-Locke solution (without glucose) with 2 ml. M/20 phosphate buffer (pH 7.4) together with about 30 mg. hexose sugars. The bottles (containing air) were closed with stoppers and incubated for 5 hours at 37°C. Following the procedure of Guha and Ghosh (*loc. cit.*) the bottles were not shaken during incubation. After incubation, 6 ml. of 10 per cent solution of trichloroacetic acid were added to each bottle and after shaking the protein precipitated was filtered off and the filtrate titrated against a standard solution of 2:6 dichlorophenol-indophenol. It is assumed that under the conditions of the experiments the indophenol titration would give the value of true ascorbic acid. It does not, however, exclude the possibility of the synthesis of non-specific indophenol reducing substances.

Preliminary experiments showed that the unminced liver was the best tissue in yielding synthesis of ascorbic acid. So in this investigation unminced slices of liver were used throughout, later. The results are shown in tables I and II.

TABLE I
Carbohydrate precursor of ascorbic acid

Carbohydrate (0.3 per cent)	Ascorbic acid synthesized mg./g. liver slices	
	Test*	Control†
Glucose ..	0.46	0.28
Mannose ..	0.30	
Maltose ..	0.32	
Lactose ..	0.23	
Xylose ..	0.28	
Sorbose ..	0.35	

* Average of two experiments.

† Average of four experiments.

TABLE II
Effect of magnesium as $MgCl_2$ (0.05 per cent) on
the synthesis of ascorbic acid in the presence of
various carbohydrates

Carbohydrate (0.3 per cent)	Ascorbic acid synthesized mg./g. liver slices	
	* Test (with mg.)	* Control (without mg.)
Glucose ..	0.83	0.46
Mannose ..	0.41	0.30
Maltose ..	0.35	0.32
Lactose ..	0.26	0.23

* Average of two experiments.

It is seen from the above that glucose, with or without the addition of magnesium, has maximum synthetic capacity towards ascorbic acid. In all possibilities it is concluded that glucose is the probable precursor of ascorbic acid in *in vitro* experiments. This observation is in conformity with that reported earlier by the author (Ahmad *et al.*, 1946) in green gram embryo seedlings. It seems to be fairly convincing that magnesium is an important link in the mechanism of which precursors (at least the sugar precursor) are converted into ascorbic acid, magnesium acting as a co-enzyme to the dehydrogenase acting on sugars.

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THE RELATIONSHIP OF THE BODY-WEIGHT TO THE WEIGHTS OF THE ORGANS

THE HEART

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As indicated in the opening paragraph of our previous paper (1949), we give below an account of our studies of the weight of the heart of a normal adult.

On carefully going through the autopsy records of the Pathology School of the Grant Medical College, it was possible to collect 109 autopsy records, where a study of the ratio of the weight of the heart to the body-weight could possibly be calculated. This group consisted of observations on 14 female and 95 male bodies. On all of these a complete post-mortem examination was performed within 18 hours of cold storage in the mortuary. In a previous paper it has been shown by us (1949) that no significant alterations in body-weights occur in such a period of cold storage. All these cases were proved at autopsy as not suffering from any gross disease or deformity; being mostly cases of accident or injury resulting in the death of a normal non-diseased person.

With further selection a much smaller group of observations was found suitable for working out the weight of the heart—28 males and only 5 females.

As the total number of 5 female dead bodies was too small for statistical study, actual organ and body-weights and the results of the calculation of the ratio of the weight of the heart to the body-weight are only shown in a tabular form without statistical conclusions in table I.

In the case of the male bodies, the results are shown in table II. It is possible, however, to study this ratio in male bodies, a little more in detail, and an attempt is made in this note to

arrive at statistically significant figures for the subject under study.

TABLE I
Females (5)

Age	Weight in kilograms	Ratio of heart to body-weight	Heart-weight, gm.
20	40.25	201.25	200
22	39.01	122.0027	290
22	55.59	346.874	160
24	39.01	208.1221	170
25	64.44	190.2932	320

TABLE II
Males (28)

Age	Weight in kilograms	Ratio of heart to body-weight	Heart-weight, gm.
18	32.64	171.36	180
18	41.76	179.375	220
18	38.61	191.1825	190
18	69.60	205.6241	320
18	39.36	195.7133	190
18	45.60	239.3996	180
20	51.78	152.91	320
20	47.01	222.261	200
20	38.4	195.3541	205
20	46.32	230.371	190
20	58.56	276.696	200
20	40.00	176.998	270
20	55.48	150.3355	350
20	45.12	203.0397	210
25	41.00	186.363	220
26	50.88	161.22	300
28	50.88	208.452	230
28	50.88	197.5164	250
28	53.76	203.2128	250
28	37.44	186.2057	190
30	46.80	221.1295	200
30	53.76	188.155	270
30	51.12	201.283	240
30	57.60	217.728	250
30	44.76	183.737	230
30	58.08	249.345	220
30	55.48	228.7708	230
30	50.88	246.933	200

The body-weight is different at different age periods. However, it remains fairly steady between the ages of 18 and 30. We could accept only 28 cases from this age group in the male for one set of observations. The range of the heart-weight in these varied from 180 g. to 350 g., the lower weights being recorded in persons with lower body-weights.

The mean heart-weight in this age group was 243.68 g. with a standard deviation of 44.08 and the co-efficient of variation of 17.27. This should give an approximate idea as to the normal weight of an adult normal heart in an average Indian male subject.

The weight of the heart is taken after washing it free from blood and clots after its removal

from the pericardial sac. Buchanan and Daly (1902) give an average weight of heart as 10.5 oz. (297.7 g.) in the male and 8.5 oz. (241 g.) in the female in the English subjects. Gray (Johnston and Whillis, 1946) states 'heart continues to increase in weight and size up to an advanced period of life and this increase is more marked in men than in women'. He mentions the average weight of an adult male heart as 280 g. to 340 g. and that of an adult female as 230 g. to 280 g. Both these English authors have met with higher weight incidence in their adult subjects as compared with our findings. No authentic Indian figures have been published so far. Mody (1947) has calculated weights of organs from dead bodies on which a post-mortem examination was held by him in the United Provinces. However, he has taken bodies of a very diverse age group varying from 10 to 70 years for his averages. Moreover, the exact number in the series is not mentioned and statistical calculations on the mean, etc., are not on record. It is possible that some of the figures refer to medicolegal autopsies in which dead bodies were brought from distances, and as pointed out in our previous paper, the state of decomposition would materially interfere in the calculation of the weights. Mody (1947) mentions the average heart-weight in the male as 10 oz. (28.3 g.) and in the female as 6.5 oz. (184.3 g.). It is presumed that the observations refer to Indian subjects exclusively.

Heart is an organ which can increase in weight in response to work load. It is evident, therefore, that these figures would not be applicable to soldiers, aviators and athletes, in a perfect normal healthy condition.

Turning to another aspect of the calculations, instead of inferring weight of the heart from the mean of actual weights in the series, a better proposition would be to establish the ratio that the weight of the heart holds to the total body-weight. This will do away with vagaries arising out of significant differences in the body-weight. With this end in view, the ratios of heart-weights to body-weights were calculated from data of 47 males (out of the gross collection of 109 and including the 28 referred to in the preceding paragraphs).

Ranges of ratios are from 142 to 291.09 and the mean of the ratios is 162.78 with S.D. of 30.86 and co-efficient of variation of 17.21.

All these figures obtained by us are lower than those obtained by European workers. Our calculations do not by any means represent a cross-section of the Indian population but they are a result of a planned study of a limited group from autopsies in Bombay over a fairly long period.

Summary

Heart-weight, body-weight and ratios of heart-weight to body-weight are presented. Statistical mean C.V. and S.D. for ratios of the

heart-weight to the body-weight and for the heart-weight separately calculated for males in age group 18 to 30 years are presented.

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EFFECT OF SULPHADIMETHYLPYRIMIDINE ON THE MICROBIAL SYNTHESIS OF THIAMINE AND NICOTINIC ACID IN HUMAN INTESTINE

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Introduction

IN recent years it has been realized that the micro-organisms of the intestine possess the capacity to synthesize a large amount of some essential vitamins which are absorbed and utilized by the host animal and that bacteriostatic agents like sulphonamides can effectively inhibit this intestinal synthesis of the vitamins. With these drugs as new tools and with improved technique of estimation, it has been shown by some nutrition experts and bacteriologists that rats can synthesize some members of B-complex, vitamins K and E in the intestine. Najar *et al.* (1943, 1944), Ellinger *et al.* (1944, 1945), Ellinger and Coulson (1944) and Oppel (1942) by conducting experiments on human subjects have reported that similar synthesis of thiamine, riboflavin, nicotinic acid and biotin takes place also in the human intestine. They have further shown that insoluble sulphonamides as sulphaguanidine and sulphasuxidine, because of their poor absorption through the intestine, induce maximum inhibition in the biosynthesis of the above vitamins of the B group. Kornberg *et al.* (1944) in course of their study of the biosynthesis of vitamin K succeeded in producing the deficiency of this vitamin in rats by using soluble sulphonamides as sulphapyrazine, sulphadiazine and sulphathiazole. By comparative study with other insoluble sulphonamides

they have found the order of effectiveness as follows: sulphapyrazine most effective, sulphadiazine and sulphathiazole next and sulphanilamide, sulphasuxidine and sulphaguanidine least effective. From the survey of the above works it is evident that the insoluble sulphaguanidine and sulphasuxidine which produce marked inhibition on the microbial synthesis of thiamine, nicotinic acid and riboflavin fail to produce any distinct effect on the biosynthesis of vitamin K in the intestine. It, therefore, appears that the inhibition of the synthesis of any particular vitamin in the intestine due to any sulphonamide is due to the specificity of the bacteriostatic action of the sulphonamides towards the different intestinal micro-organisms that take part in the synthesis of the vitamins. Investigation has, therefore, been begun in this laboratory to study how the different sulphonamides available in the market behave in inhibiting the biosynthesis of thiamine, nicotinic acid and other members of B-complex and also to study the actual mechanism of inhibition.

For systematic survey, the sulphonamides so far prepared may be classed under three major groups:—

(A) *Insoluble in water, acid and alkali.*—Sulphaguanidine, succinylsulphathiazole and phthalylsulphathiazole.

(B) *Soluble in acid and alkali but sparingly soluble in water.*—Sulphadiazine and sulphadimethylpyrimidine.

(C) *Soluble in water, acid and alkali.*—Sulphanilamide, sulphathiazole, sulphapyridine and sulphapyrazine.

Since much work had been done with the sulphonamides of group A, our attention was directed to the study of those of groups B and C and in the present communication, which represents the first of the series of works begun here, sulphadimethylpyrimidine—a typical member of the sulphonamides of group B—has been selected to investigate its effect on the microbial synthesis of thiamine and nicotinic acid in the human intestine and also to see whether the application of this drug interferes with the absorption and storage of the above vitamins.

Experimental

Experiments were carried out on five adult human subjects of ages varying from 25 to 40 years and of weights varying from 45 to 53 kilos. They were kept under proper care and strict observation in the hospital and were given daily the weighed amount of the basal diet for the whole of the experimental period which lasted from eighteen to twenty-four days.

In experiment no. 1 the subjects were first fed on the basal diet and after a preliminary period of three days the 24 hours' urine was collected for a further period of three consecutive days on that basal diet and their thiamine contents

were measured. After this the basal diet was supplemented with daily dose of 3 gm. sulphadimethylpyrimidine ('sulphamezathine' of Imperial Chemical Pharmaceutical, Ltd.) in three equal doses (each dose two tablets of 0.5 gm.) after an initial dose of 3 gm. The urine on this supplement was collected for a period of three days after a preliminary period of same days on this drug. To see whether the above sulpha drug supplement interfered with the absorption and storage of thiamine, a test dose of 5 mg. of thiamine was then given along with the above drug and the urine on such double supplements was collected for a period of three consecutive days after same preliminary period as before. The recovery of the test dose of the above vitamin under the influence of the above sulpha drug was then compared with that when the test dose was given alone with the basal diet without the sulpha drug supplement as carried out in experiment no. 3. The influence of the above sulphadimethylpyrimidine on the biosynthesis of nicotinic acid has been studied in another set of experiment no. 2 and this was carried out in a manner similar to that adopted in experiment no. 1 except that in this case the test dose used was 300 mg. nicotinic acid and the recovery of this test dose with sulpha drug was compared with that when it was used without sulpha drug as in experiment no. 4.

Thiamine and nicotinic acid of the urine were measured according to the following methods:

Thiamine.—This was estimated by the base exchange technique using 'Decalso'™ as selective absorbent according to the method of Hennessy and Cerecedo (1939) as modified by Brown *et al.* (1943). Decalso was used for adsorption and purification of thiamine.

Nicotinic acid.—This was estimated after hydrolysis with acid, and with alkali and urea according to the method of Swaminathan (1942) with some alterations based on the technique of Wang and Kodicek (1943) and the values represent nicotinic acid, nicotinamide and nicotinic acid, and also trigonelline in which N-methyl-nicotinamide—an important product of nicotinic acid metabolism in urine—is also included and all these have been expressed as total nicotinic acid.

The chronological order of the experimental periods is denoted by the arithmetical numbers as P-II, P-IV, etc., and the periods which do not figure in the tables must be assumed to be the preliminary periods for the succeeding ones. The results of the above four experiments have been summarized and presented in the table.

Results

Effect of sulphadimethylpyrimidine on the biosynthesis of thiamine.—It is observed from the results of experiment no. 1 that the urinary

* Decalso F used for the estimation of thiamine was received from Messrs. Permutit Co., Ltd., England, to whom our thanks are due.

TABLE

Effect of sulphadimethylpyrimidine on thiamine and nicotinic acid excretion in five normal human subjects. The figures indicate the daily average values of an individual. Basal diet composed of 550 to 600 gm. rice, 70 gm. pulse, 70 gm. fish, 200 gm. vegetables, 30 gm. mustard oil, and 4 oz. milk twice a week

	Period	Diet and supplement		URINARY ELIMINATION	
				Range	Mean
Experiment no. 1. Experiment with sulpha drug and sulpha drug + test dose of thiamine.	P-II	Basal diet	Total B ₁ in μ g. per day	98.0 - 138.0	120.0
	P-IV	Basal diet + 3 gm. sulpha drug.	Do.	18.0 - 32.0	25.0
			Per cent reduction of elimination due to sulpha drug.	73.3 - 84.2	78.8
	P-VI	Basal diet + 3 gm. sulpha drug + 5 mg. test dose of thiamine.	Total B ₁ in μ g. per day	643.0 - 838.0	725.0
			Per cent recovery of the test dose.	12.3 - 16.1	14.0
Experiment no. 2. Experiment with sulpha drug and sulpha drug + test dose of nicotinic acid.	P-II	Basal diet	Total N.A. in mg. per day.	6.09 - 8.33	6.95
	P-IV	Basal diet + 3 gm. sulpha drug.	Do.	11.34 - 14.91	12.98
			Per cent reduction of elimination due to sulpha drug.	72.3 - 100.2	86.9
	P-VI	Basal diet + 3 gm. sulpha drug + 300 mg. test dose of nicotinic acid.	Total N.A. in mg. per day.	71.86 - 82.21	76.72
			Per cent recovery of the test dose.	19.1 - 24.0	21.2
Experiment no. 3. Test dose experiment with thiamine.	P-II	Basal diet	Total B ₁ in μ g. per day	102.0 - 132.0	115.0
	P-IV	Basal diet + 5 mg. thiamine as test dose.	Do.	733.0 - 919.0	877.0
			Per cent recovery of the test dose.	12.4 - 17.2	15.2
Experiment no. 4. Test dose experiment with nicotinic acid.	P-II	Basal diet	Total N.A. in mg. per day.	6.18 - 7.24	6.42
	P-IV	Basal diet + 300 mg. nicotinic acid as test dose.	Do.	62.77 - 78.53	72.60
			Per cent recovery of the test dose.	18.5 - 21.1	22.0

The subjects employed were : B. S.—body-weight 49 kilos, age 29 years.

M. R.— " 48 " " 32 "
 A. D.— " 45 " " 25 "
 B. M.— " 53 " " 40 "
 S. T.— " 46 " " 30 "

thiamine excretion of the five subjects on the basal diet ranged from 98 to 138 μ g. with the mean value of 120 μ g. After oral administration of 3 gm. of sulphadimethylpyrimidine for six days the daily excretion of the above vitamin in the urine decreased to the limit of 18 to 32 μ g. with the mean value of 25 μ g. The average per cent reduction in the elimination of thiamine under the influence of the above sulphonamides was found to be 78.8 when the subjects were then given a test dose of 5 mg. of thiamine along with the above sulpha drug in the succeeding periods P-V and P-VI so as to determine as to whether the ingestion of the drug in the

previous periods along with the basal diet only affected the absorption and storage of thiamine; it was found that 12.3 to 16.1 per cent of the ingested test dose was recovered in the urine and these values almost corresponded to those obtained in another experiment no. 3 after ingestion of similar test dose of thiamine without the above sulphonamide supplement. That the above sulpha drug also does not interfere with the estimation of thiamine by fluorimetric method is evident from the fact that the thiamine contents of the samples of normal urine did not show any variation even when the sulphonamide was added to them.

All the above observations clearly indicate that the reduction of thiamine excretion as obtained after oral administration of sulphadimethylpyrimidine in period IV of experiment no. 1 is not due to interference with the absorption and storage of thiamine but may be ascribed as due to decrease in the biosynthesis of this vitamin in the intestine resulting from the inhibition of the growth of those species of micro-organisms which lead to the synthesis of a large amount of this vitamin in normal conditions.

Effect on nicotinic acid synthesis.—In experiment no. 2 it has been found that the subjects on basal diet excreted from 6.09 to 8.33 mg. or with the mean value of 6.95 mg. of nicotinic acid daily in the urine. Unlike the previous experiment, the oral administration of sulphadimethylpyrimidine in daily dose of 3 gm. in this case led to the increase of the urinary elimination of nicotinic acid to an enormous extent—the range being 11.34 to 14.91 mg. with the mean value of 12.98 mg. per day. The percentage increase of the nicotinic acid excretion due to administration of the above sulphonamide was found to vary from 72.3 to 100.2 with the mean value of 86.9. When the test dose of 300 mg. nicotinic acid was given to the subjects along with this sulphonamide the percentage recovery of the added test dose was found to lie between 19.1 and 24.0 with the mean value of 21.2 and this value corresponds with that obtained in experiment no. 4 by administering similar test dose without any sulphonamide. This shows clearly that the oral administration of sulphadimethylpyrimidine does not interfere with the absorption and utilization of nicotinic acid in the body. It has further been observed that the addition of this sulphonamide to the urine does not affect the colour reaction in the estimation of nicotinic acid by the cyanogen bromide reagent. So it seems evident that the increased elimination of nicotinic acid after oral administration of the above sulphadimethylpyrimidine is due to increase in the availability of the total nicotinic acid synthesized by the intestinal flora.

It is suggested that under normal conditions a competition exists between the microflora which synthesize and those which destroy or utilize nicotinic acid and other vitamins for their growth. Most probably the above sulphonamide inhibits the growth of the latter species of micro-organisms of the intestine and thus releases a fair amount of nicotinic acid, which would otherwise have been utilized by these micro-organisms for their metabolic activities, for absorption through the intestine and for utilization within the body of the human subject.

The results presented in the table also give some indication as to the total amount of nicotinic acid synthesized daily in the human intestine. Fifty to 80 per cent reduction in the urinary elimination of nicotinic acid—which amounts to about 3 to 4 mg.—due to oral inges-

tion of sulphaguanidine and sulphasuxidine as observed by Najjar *et al.* (*loc. cit.*) and Ellinger *et al.* (*loc. cit.*) represents only a portion of the total synthesized acid left unutilized by other species of intestinal micro-organisms. From the results of the present investigation it is observed that after oral administration of sulphadimethylpyrimidine to the adult human subjects there is an increase in the elimination of nicotinic acid by about 6 mg. and this value represents the amount of the synthesized acid which is destroyed or utilized by some micro-organisms in the intestine in the normal conditions. So the minimum quantity of nicotinic acid synthesized daily in the human intestine is between 9 to 10 mg.

Discussion

Micro-organisms which take part in the synthesis of vitamin B₁ do not require it as a growth factor in their medium and the vitamin B₁ synthesized by them functions as an essential metabolite taking part in the various enzymatic reactions required for their growth. Since both thiamine and sulphadimethylpyrimidine, used in the present investigation, contain a common pyrimidine ring it seems that the decrease in the elimination of thiamine after oral dose of the above sulphonamide is probably due to inhibition of the growth of the thiamine synthesizing intestinal microflora as a result of diffusion of this sulphonamide within their cells and of interference with the essential enzymatic reactions by competition with the enzyme constructed from vitamin B₁. The competition with another essential metabolite p-amino-benzoic acid as postulated by Fildes (1940) may also be partly responsible for the above inhibition of the growth of thiamine synthesizing bacteria.

The increased nicotinic acid elimination observed after oral administration of the above sulphonamide may be explained in the following ways :

1. It is not unlikely that the micro-organisms which synthesize thiamine require for their growth nicotinic acid which is available from the large store synthesized by other species. As an example it may be cited that propionic and lactic acid bacteria (some species and strains), *dysentery bacilli* and *C. diphtheriae* are able to synthesize thiamine but require nicotinic acid as the growth factor in their medium. So in the present investigation when the sulphadimethylpyrimidine is administered the growth of the thiamine-synthesizing micro-organisms is inhibited and large amount of nicotinic acid required for their metabolic activities is thus released for absorption and utilization by the human body.

2. Other species of micro-organisms not synthesizing thiamine may also be present in the intestine which require in their medium, in addition to nicotinic acid, also vitamin B₁ which is available both from the endogenous source, *i.e.*

from the micro-organisms which synthesize this in the intestine and also from the exogenous dietary source. When the above sulphonamide is administered the endogenous source is stopped as a result of inhibition of the growth of the vitamin B₁ synthesizing micro-organisms according to the mechanisms discussed above and the exogenous dietary source seems to be blocked extracellularly by the drug and thus when all the available sources of thiamine are stopped, the growth of the above species of organisms is inhibited and a large amount of nicotinic acid is thereafter released for absorption and utilization by the human body. Similar blocking has also been suggested by Knight (1945) in explaining the inhibition of the growth of *Lactobacillus arabinosus* (requiring nicotinic acid for growth) after addition of sulphapyridine in the medium as observed by Tepley *et al.* (1943).

From the above discussion it is evident that the sulphadimethylpyrimidine although highly soluble in acid and alkali exerts its bacteriostatic action on those micro-organisms which synthesize thiamine and which utilize or destroy nicotinic acid in the intestine. It may, therefore, be postulated that the capacity of any particular sulphonamide inhibiting the microbial synthesis of the vitamins in the intestine depends not only on the rate of absorption through the intestine but also on the specificity of the bacteriostatic action of the drug towards the micro-organisms involved in the process of biosynthesis of the vitamins. This antibacterial action is dependent on its structural relationship with the growth factor or the essential metabolite of the different micro-organisms that take part in the biosynthesis.

Summary

1. Oral administration of sulphadimethylpyrimidine to five adult human subjects decreased the average urinary elimination of thiamine from 120 to 25 μ g. The average percentage reduction was found to be 78.8.

2. In case of nicotinic acid the average urinary elimination was found to increase from 6.95 mg. to 12.98 mg. and the average percentage increase was calculated to be 86.9.

3. The recovery of the test dose of thiamine and nicotinic acid administered with and without the above sulphonamide supplement has revealed that this drug does not interfere with the absorption and utilization of the above vitamins.

4. The decreased elimination of thiamine and increased elimination of nicotinic acid due to ingestion of the above sulphonamide are probably due to inhibition of the growth of those micro-organisms which synthesize thiamine and those which utilize or destroy nicotinic acid and the mechanism of the inhibition has been discussed.

5. From the data obtained in the present investigation the minimum quantity of nicotinic acid synthesized in the human intestine has been calculated to be 9 to 10 mg.

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CLINICAL HYDROPHOBIA WITHOUT CONTACT WITH RABIES-TRANSMITTING ANIMAL

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It is universally believed that clinical hydrophobia occurs in man only after coming in contact with a rabid animal. The virus of rabies is transferred by the saliva of such an animal to a raw surface on the human body and clinical symptoms of hydrophobia may appear after a varying incubation period of about three months, though in some instances, the latter period may be greatly prolonged. Two cases reported below and three others seen in private practice have tended to shake the writer's belief in the accepted method of the transmission of the virus by the bite or licking by an infected animal as the only mode of infection, and have set him thinking whether there may not be some other mode of transference of the virus.

Case 1

A male, aged 45, policeman by occupation, was admitted to the Sassoon Hospitals, on 6th February, 1949, for giddiness and breathlessness of a few hours' duration. He ascribed his complaints to injection and medicine given to him two days back for another complaint. When he was admitted, he was restless, and unable to walk and talk properly. His breathing was hurried and embarrassed. He incessantly sat up in bed and tried to jump over the railings of the cot. His systemic examination revealed nothing abnormal. During examination, a ward boy was standing by with a bowl of lotion. After finishing the examination, as the bowl was lowered to wash the writer's hands, the patient, at the sight of water inside, went into a typical hydrophobic spasm with convulsive movements of the extremities accompanied by great mental excitement. This gave the clue, and for confirmation, when water was offered to him for drinking, the spasmodic seizure with the mental phenomenon was repeated. Gradually he became more boisterous, talked incoherently when asked, and died at 3-15 p.m. on the 8th in a fit of hiccough. He gave no history of a bite or even a contact with a rabies-transmitting animal, on repeated and direct questioning. His relatives said that there were no such animals in the neighbourhood or in the house.

Case 2

A male, aged 30, a mechanic by profession, was admitted to the Sassoon Hospitals, on 6th July, 1949, for restlessness, insomnia and 'peculiar behaviour' since the previous day. Occasionally, he appeared greatly excited. Physical examination revealed nothing abnormal. The history, as obtained from the patient, his father and his wife, was as follows: He returned from his workshop in the evening on 5th July, 1949, complaining that he was not feeling well and desired to go to bed. His wife offered him tea and food but he would not take anything, though he said he was hungry and thirsty. His wife thought that a night's rest might relieve him in the morning, but to her surprise, he was restless the whole night and did not sleep. In the morning he appeared to be more irritable and easily excited. When he tried to take tea in the morning, his wife observed 'peculiar behaviour' on his part. So his father brought him to the hospital. On admission it was found that he was well-built and strong, and appeared as if scared of something. Sometimes he appeared greatly excited, would sit up and even try to jump from over the cot. During the lucid moments, he was closely interrogated about any contact with rabies-transmitting animals, but no such history could be elicited from him or his relatives. During examination, he complained of great thirst. So water was called for, and as if,

to confirm our suspicion about hydrophobia, he showed typical 'hydrophobic phenomenon', when he saw the water. He could not drink any, and in excitement, he threw the pot away. Similar further proof of the clinical diagnosis of hydrophobia was available during the course. The patient was kept under observation, but he showed greater mental agitation and more severe fits of spasms and died the same evening.

Comments

The cases reported above were obviously those of clinical hydrophobia. The possibility of alternative diagnosis like mania, hysteria, atropine or belladonna poisoning, etc., was considered and ruled out by the facts and the physical examination in each case. Unfortunately, it is difficult to obtain permission for post-mortem examinations in our country. Hence, we are forced to depend solely on the clinical course of the disease for diagnosis. Both cases were from the city and significantly lacked the history of contact with infected or healthy rabies-transmitting animals, though directly and repeatedly questioned about it. Under these circumstances, it is usual to presume conveniently that the contact with a rabid animal may be so insignificant as to be easily forgotten. The writer cannot contribute to the presumption in the above cases because he does not believe that, in city life, a contact with an animal, particularly a rabid one, is so insignificant an affair as to be easily forgotten and not recollected even after repeated and direct interrogation about it. In addition, both the patients were intelligent and educated, and were aware of the consequences of such a contact and would not have ignored it by going without the necessary prophylactic treatment. The presumption is that the above quoted cases were clinically hydrophobia produced without a contact with rabies-transmitting animal.

Discussion

If it is accepted that in these cases there was no direct transmission of the virus from the animal to the man, one is left with the only possibility of indirect transmission to produce the human infection. This may be possible in one of the following ways:—

1. By way of air, i.e. air-borne infection.
2. By contact with dry infected articles.
3. By contact with, or ingestion of, infected water.

Before discussing the above possibilities, it will be useful to mention some of the proved data regarding the virus. The virus is very susceptible to drying and loses its virulence in the process. For successful implantation, the virus must be implanted on nervous tissues. Thus infection is not possible without a breach of surface in the skin or mucous membrane. Wounds and abrasions which have granulated

for more than 24 hours may be taken as unbroken surface.

As the virus loses its virulence by drying (the first two of the suggested modes of infection) *viz*, (1) air-borne infection, and (2) infection by contact with dry infected articles, appear to be improbable at least in the tropics, even though a breach in the skin surface may be present. The third suggested mode of possible infection, *viz*, by contact with, or ingestion of, infected water is worth considering. The virus may remain unattenuated for long in water, because the chances of drying are remote. A rabid animal being thirsty, may approach water, and as it is unable to swallow, may inadvertently infect the water in a vessel by its infective saliva, which may trickle down (due to inability to swallow). A breach in the skin or mucous surface may come in contact with the infected water, during washing, or drinking. Raw surface in the mucous membrane of the mouth and nose, in particular, is perhaps as common, if not more, as in the skin. Though, perhaps the virus may be destroyed in the stomach, the raw oral and nasal mucous membranes deserve consideration as portals of entry of the virus. It is for the experimentalists to explore the possibility of such a water-borne infection.

It will also be essential to investigate whether a 'carrier' state for rabies exists in animals. If it is so, a susceptible animal may appear normal, and yet its saliva may be infective. Thus, the danger of direct transmission and the above postulated 'water-borne' infection may be increased.

In view of the uniformly and rapidly fatal outcome of the disease after the symptoms have once appeared, little advance has been made in the methods of diagnosis and treatment of this serious malady, since the days of Pasteur. There is an urgent need for research along the line, as the occurrence of human rabies in India does not appear to be very uncommon.

Conclusions

From the two cases observed in the hospital and three others in private practice, it is suggested that an indirect mode of transmission of the rabies virus to the human being probably exists. This may be by means of home water infected by the saliva of a rabid animal. The infection in the human being may take place by the infected water coming in contact with a raw surface in the skin or the mucous membrane, particularly of the upper alimentary tract and the nose.

Summary

Two cases of clinical hydrophobia without any direct contact with rabies-transmitting animal are described.

In addition to the direct transmission of the rabies virus as a mode of human infection, the

probability of an indirect 'water-borne' infection is postulated.

Need for investigation into the possibility of a 'carrier' state in susceptible animals, and in the methods of diagnosis and treatment of this serious and relentlessly fatal malady is stressed.

Addendum

After the above article was despatched for publication, the author read with interest that . . . 'rats are susceptible to rabies, and theoretically constitute a possible reservoir and source of infection for man' (Willmoth, 1949). Though in the above reported cases there is no history of rat bite (as confirmed from relations), a number of cases where a history of contact with the usual rabies-transmitting animals is not obtained, may be attributable to a rat bite.

I am thankful to the Civil Surgeon, Poona, for his kind permission to publish the above case reports of patients admitted to the Sassoon Hospitals under me.

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PENICILLIN IN GUINEA-WORM INFECTION

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THOUGH various indigenous drugs have been reported to be useful for guinea-worm infection, nothing has been found to be specific. The author had occasions to see cases of guinea-worms being treated by quacks with different indigenous drugs. He observed that certain drugs had good results on a few cases and none on others. The common treatment in the number of villages is of extraction by suction with a locally made suction apparatus of metal. Some of these so-called guinea-worm surgeons are quite expert at their job and take out the worms by skilful massage and suction, but there is fraud in it too. In order to get more money, they keep some guinea-worms hidden somewhere and show a much larger number than what they have actually extracted.

Those who treat guinea-worm patients by internal medication have been mostly found to be doing this work out of philanthropic motives. They do not charge any fee and give medicines also free of cost. By close contact with some of these persons the author found that the following indigenous drugs have generally been used :

1. Small marking-nut wrapped in *gur* to be swallowed whole for one or two days. The patient is asked to avoid any kind of heat and should remain in a cool place.

2. Burnt lime is powdered and given in curd for 3 days.

3. Alum is given in betels.

4. Acid benzoic in betels.

5. Acid arsenous in lime juice applied externally on the protruded guinea-worm.

Besides these, there are certain other drugs which are used, but their names are not disclosed. Unfortunately no scientific investigations have been made regarding the use and abuse of these indigenous drugs and no specific remedy is yet found out. This is the reason why guinea-worm patients generally do not come to the hospitals or dispensaries till surgical intervention becomes necessary due to abscesses, cellulitis, ankylosis, etc. Unlike what happens in the case of other worms, no symptoms causing inconvenience, discomfort, or pain are observed excepting urticaria and mild toxic symptoms, when the worm tries to come out on the surface of the body.

Penicillin has been tried in hospitals on cases of guinea-worm cellulitis with good response for secondary infection, but with no action on the worm has been reported.

Experiment was made on a case of broken guinea-worm by injecting penicillin at the local site with very good result. It was tried on 4 more cases subsequently with the result that patients were completely cured during the course of one to two weeks. Out of these 5 patients three had cellulitis due to the breaking of the worm during the process of extraction. In the remaining two the worm had not made any opening and was found under the skin. In all these cases penicillin G solution, 25,000 units, was injected at the local site every day in the area of swelling or by the side of the worm. In all these cases the worm became thinner and thinner and disappeared completely without causing any pain, swelling or discomfort. All these patients were discharged from the hospital within 8 to 15 days excepting the first two cases who were kept for observation for a longer time. Further trials will be made but the main idea of publishing this is to request colleagues who may be working in areas where there may be a good number of guinea-worm cases available to try penicillin in different strengths, at shorter intervals, and also to inject into the body of the worm and to see the effects of all these trials and publish them for the information and guidance of others.

Case reports

1. Patient, aged 30 years, head constable police while on the usual parade, suddenly felt giddy and fell down and was removed to the hospital. Within a few hours of his admission urticaria and signs of nausea were observed. Next day the rash disappeared and a blister was observed on the outer side of the right leg and on examination guinea-worm could be felt in the leg. Gradual extraction of guinea-worm was

undertaken. Nearly three-fourths of the worm was extracted within about 8 days and unluckily it was broken. Next morning the leg was found slightly swollen and painful. It struck me to try penicillin and a watery solution of penicillin G was injected at the local site and a few drops were put in the open wound through which guinea-worm was coming out. Next morning the pain and swelling were found to be less. This treatment was continued for a week, i.e. injecting penicillin 25,000 units in the leg at different sites round about the ulcer. The remaining portion of the broken worm and slight amount of pus caused by the discharge of ovas came out easily. The wound healed and the patient was saved from the discomfort, pain and swelling which usually last for days.

2. A patient named Ditya, aged 30 years, had guinea-worm on the back of the thigh. More than half was extracted and then it was broken. Penicillin, 25,000 units, was injected at the local site. The patient had no pain, nor any swelling in the thigh, but he complained of pain in the abdomen after 12 hours. On examination a diffused swelling in the abdominal wall extending from the right iliac fossa to the symphysis pubis was found. It was inflamed and tender. Penicillin 25,000 units was injected at the site and antiphlogistine applied. The inflammation and the diffused swelling subsided, and now a cystic tumour of the size of an egg was felt. The treatment was continued for 5 days by which time the tumour was reduced to the size of a plumb. The patient left the hospital.

3. Kubersing Naharsingh, aged 22 years, was admitted on 12th August, 1949, for swelling, pain and inability to extend left knee for about a week. He had a number of guinea-worms in both the ankle joints for a year. Some were extracted and some were treated with indigenous external applications. One month previously a guinea-worm had come out from just below the left knee after the usual symptoms of urticaria and blister at the local site. It was being extracted gradually by a guinea-worm expert. About a fortnight before his admission the guinea-worm was broken. Some pieces came out by local application, but certain portion remained inside, causing the present symptoms.

On admission he had synovitis and tenderness in the lower part. He could not extend the leg due to the swelling, but the movements of the knee joints were free and painless in semiflexed position. The opening through which the guinea-worm had come out had healed.

On admission he was put on salicylates, ichthyol and glycerine locally. No improvement was noticed till 14th, when everything was stopped and he was put on penicillin G injection 25,000 units on the swelling. Within 24 hours improvement was noticed. Within 4 days the swelling had gone down 50 per cent and the patient could extend the leg without much pain. Six more injections made him all right and he could

walk, sit and do all his work without any pain or discomfort.

On the tenth day of penicillin treatment the swelling had completely disappeared and the patient was discharged cured.

4. A patient admitted for some other ailments got a blister on his right leg and guinea-worm could be seen round about his right ankle. Without disturbing the blister penicillin was injected on the sides of the guinea-worm which could be seen and felt. About half an inch of the guinea-worm came out of the blister which had burst. Antiseptic dressing with cold pad was applied and no attempt was made to extract the worm. The guinea-worm was found becoming thinner and thinner and could not be seen or felt after 5 injections of penicillin. The portion of the worm that had come out through the opening was found in the dressing on the second day and the opening closed within 3 days. Three more penicillin injections were given at different sites locally and the patient was discharged symptom- and pain-free.

5. A patient, aged 20 years, was admitted for chronic malaria and anæmia. One day he showed a guinea-worm in the right forearm and wrist. Penicillin injections were started as usual and within 10 days the worm disappeared completely.

Conclusions

1. Penicillin injection locally at the site of the guinea-worm has proved efficacious in killing the worm which later on is probably absorbed.

2. The dead worm or the ova of the broken worm are thrown out if there is already an opening in the skin, or are absorbed.

3. The secondary infection and the complications arising out of it are all avoided.

4. Further trials may reveal that stronger doses or 4 to 8 hourly injections might reduce the period of treatment.

5. Treatment can be given even in the out-patient department, as there is no swelling, pain or discomfort, and the patients can walk and come for treatment.

I express my grateful thanks to Colonel Shankarlal Gargye, L.R.C.P., M.R.C.S., Director of Medical and Health Services, Madhya Bharat, for permitting me to publish this article.

A Mirror of Hospital Practice

AUREOMYCIN IN THE TREATMENT OF TYPHOID FEVER

By SURESH CHANDRA BHATTACHARYA, M.B.
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My son, aged 12 years, was attacked with slight fever with headache on the 19th August,

1949. After five days of illness during which temperature was not properly recorded, he was confined to bed with severe headache and fever, temperature varying between 101°F. and 103°F. From that day his fever gradually increased and by the 9th day the temperature was 102°F. in the morning and 103.6°F. in the evening. This remittent type of temperature continued, till on the 14th day it was between 103.4°F. and 104.6°F. His only complaint was severe headache. The patient was apathetic and very drowsy from the end of the first week. His pulse was between 90 and 100 per minute of low tension. There was rash on the face, chest and abdomen on the 9th day and enlarged, slightly tender cervical glands were noticed on the same date. Respiration was about 30 per minute. Face flushed, tongue furred with red margins and moist, abdomen slightly tumid, liver and spleen not palpable, bowels constipated. Heart and lungs—nothing particular noted. Blood was examined on the 9th day for total and differential counts and the report was as follows :

Hb. 65 per cent, total R.B.C. 4,220,000 per c.cm. Total W.B.C. 5,400 per c.cm. Differential count : polymorphs 72 per cent, small mono 28 per cent, large mono nil, eosinophils nil, other abnormal cells nil, malaria parasite none found.

The only marked feature of the patient was that he was very drowsy and, in fact, in stuporous condition till the 14th day of illness. Clinically, I diagnosed the case to be of enteric fever and treated him accordingly.

From the 15th day I started giving him this new antibiotic aureomycin, known to be very effective in typhoid fever by some observers.

On the morning of the 15th day at 8 a.m. the temperature was 103.4°F. and I gave him orally one capsule of aureomycin hydrochloride 250 mg. (Lederle) and repeated the dose every 3 hours. At 11 a.m. the temperature rose to 104.4°F. when the second capsule was administered. Shortly after that perspiration appeared and the temperature came down to 103.4°F. I continued giving the capsule regularly every 3 hours and temperature rapidly came down with profuse perspiration and at 8 p.m. in the evening when the 5th capsule was administered, the temperature was 99.4°F. At 11 p.m. I stopped giving him further capsules since the temperature was at that time 98°F. and the patient was very weak and bathed in perspiration with slow pulse of very low tension. I gave him 1 grain coramine, 15 drops every ½ hour for two doses. During these 12 hours the patient passed copious urine (clear), there was no flatulence and his drowsiness gradually disappeared but he seemed to be very weak. Next day his general appearance improved much, there was no further rise of temperature and perspiration continued. I gave him two more aureomycin capsules in the next 24 hours and one capsule the day after. Thus I

administered 8 capsules in all in 48 hours. The patient rapidly recovered. His tongue became clear, bowels moved, urine clear and copious and clinically he was immensely better within 48 hours. As a matter of fact, I found him normal in all respects within two days of starting aureomycin. This remarkable effect cannot but impress any unprejudiced observer. I think this wonderful drug deserves fair trial in all cases of enteric fever so that one can properly assess the therapeutic effect of this new antibiotic.

[Clinically typhus is not ruled out.—*Edron, I.M.G.*]

PLAGUE COMPLICATING ENTERIC FEVER

By P. K. GHOSH, M.B.

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TYPHOID and plague are both serious diseases and in spite of up-to-date treatment they take a heavy toll of human lives. The seriousness, when these two maladies combine in one individual, can be well imagined.

Recently, I had to treat such a case in a village where any laboratory help or consultation with any other doctor is rather a matter of dreams. The case, however, was saved rather unexpectedly in a very short time with dihydrostreptomycin sulphate and sulfadiazine.

The village Babhnan market (District Basti) has been an endemic area for plague for a long time. Most of the inhabitants are not inoculated and the locality is very unhygienic, dirty and dingy. All the different forms of plague are encountered here, bubonic variety dominating others.

A Hindu girl, aged 13 years, was being treated by a *hakim* for enteric fever. On 4th September, 1949 (19th day of illness), her axillary temperature shot up to 106°F. in the morning with restlessness and incoherent talks. Her condition became worse in spite of measures adopted by the *hakim* and I was called in to see the case at 6 p.m. on the same afternoon.

She was found to be a textbook case of enteric fever with the typical rash extending to the lower abdomen. She was highly toxæmic, almost unconscious with hurried pulse and respiration rate, axillary temperature of 106°F. and glandular swelling with 'rubor and dolor', both in the cervical and the inguinal regions, without any apparent cause to account for the inflammation.

She was given a glycerine enemata to relieve her bowels constipated all these 19 days. Ice being unavailable, Eau-de-Cologne water was applied on the forehead. Diaphoretic mixture

suitable for the condition and 1 gm. sulfadiazine per dose was prescribed four-hourly along with copious glucose drinks. Belladonna plasters were applied locally. Dihydrostreptomycin sulphate could be procured next morning and 0.5 gm. in 2 cc. normal saline was injected at 9 a.m. on 5th September, 1949. At 9 p.m. I saw her again. She appeared better in all respects and her axillary temperature was 103°F. 0.25 gm. dihydrostreptomycin in 2 cc. normal saline was repeated at 9 p.m. and continuation of the mixture and other treatment was advised with copious fluid intake.

Surprisingly enough, she was found to be afebrile (97.2°) with extreme weakness and prostration. Injection was withheld and stimulants were given. She recovered in no time and continued making steady progress and her subsequent treatment needs no comment.

A CASE OF TETANUS TREATED WITH PENICILLIN

By AMRIT LAL WAHI, M.B., B.S.

CAPTAIN

Deog. (Bharatpur State)

On 23rd May, 1949, a young woman, aged 25, was admitted to the hospital with the complaint of a sinus, discharging pus on the left buttock, of 3 months' duration. The history of the case was that three months back an abscess appeared on the left buttock which burst after a few days. The discharge of the pus then commenced.

Past history.—She had had similar trouble thrice in the last nine years and was operated upon for it several times with varying results.

Condition on examination.—1. *Local:* The opening of the sinus was situated at the left gluteal fold, was $\frac{1}{2}$ inch \times $\frac{1}{2}$ inch in size, was discharging pus and was covered with exuberant unhealthy granulations. Probe could be pushed in 3 different directions to the extent of 1 inch to 2½ inches. The probe did not touch bone anywhere.

2. *General examination.*—General condition of the patient was fair. Teeth and tonsils were normal and there was no evidence of tuberculosis.

Treatment.—On 25th May, 1949, the operation was performed under chloroform general anaesthesia. The tracts of the sinus were opened up and scraped with a sharp scoop. The wound was dressed. On 27th May, 1949, the patient suddenly complained of inability to open the mouth. As the teeth and tonsils were normal, she had no other complaint and the sort of lesion on which she had been operated being particularly favourable for the abode of *Cl.*

hand and bowl of sacred water in the other. She was worshipped together with Asklepios and regarded as his daughter. The cult of Hygieia spread concurrently with that of Asklepios and was introduced in the temples at Rome from Epidaurus in 293 B.C., while in classical times Asklepios and Hygieia are simply the god and goddess of health. In the declining years of paganism they were considered as the protecting deities.

3. *Artemis*.—She is one of the principal goddess in Greek mythology and is considered a counterpart of the Roman Diana. She is the daughter of Zeus and Leto, twin sister of Apollo. She is the goddess of chastity, protectress of young men and maidens and is stated to deal with death, and also along with Apollo she is a healing and a purifying divinity—*Oukia* ('the healer' c.f. Apollo aulios).

The serpents as healers of illness

Healing power of serpents is very familiar in all legends. In mythology Siegfried bathed himself in the blood of the dragon he slew and thus became invulnerable. The Odosius recovered eyesight when a grateful serpent laid a precious stone upon his eyes. Cadmus and his wife were turned into snakes to cure human illness. Serpents were tended in the sanctuaries of Greek Aesculapius (Asklepios). The serpent father of Alexander the Great came with a healing root to cure one of his generals. It was a popular belief that the healing skill could be gained by eating some parts of a snake. A walking stick from a species of cane grown in the neighbourhood of a serpent-god shrine is believed to protect against snake bites. At Farnando when there was a epidemic among children they were brought to touch a serpent's skin which was hung on a pole. In Kashmir the serpent tribes are famous for their healing skill in general and they attribute their skill as derived from the snakes.

Serpents as an emblem of the medical profession

As far as the recorded history of medicine goes it seems to show a very close association of serpents with the art of healing. The Sumerian vase which dates from 2350 B.C. and was dedicated by Gudea of Babylon to Ningishzida, son of Ninazu, the master physician, is always associated with Asklepiian monuments. The species of snakes depicted under the throne of Asklepios is recognized as *Coluber longismus* (Aesculapius). This species is named after god Asklepios by Aldrovandi of Bologna (1522-1605) and has generally been regarded as the true serpent of Asklepios (see figures 4 and 5, plate XXXII). This snake is found in various parts of Europe.

Figure 6, plate XXXII, is a photograph from a painting taken from the front page of Seminar (1948). The picture shows a hawk,

two green snakes coiling around a staff, a dagger thrust into the heart of the hawk and a woman sitting besides these. The hawk represents the ancient symbol of death and here it represents a predatory rendering destruction, a cancer. The serpents represent a timely medical aid and the dagger in the heart of the hawk, the surgical operation, giving the victim (woman) a timely aid and who has been spared death and has found the difficult but not the impossible path leading to a continued useful life.

Caduceus

Mythologically, Caduceus represents the rod carried by Mercury, the messenger of gods. It is shown as a wand surmounted with two wings and is entwined by two serpents. Caduceus is a latin adoption of a herald's wand—a staff carried by messengers when on heraldic missions. In its oldest form it was a rod ending in two prongs (probably an olive branch with two shoots) adorned with ribbons and garlands. Later on probably two serpents with heads meeting at the top of the staff replaced the ribbon. Historically, the Caduceus was the attribute of Hermes, the god of commerce and peace, and among the Greeks it was a distinctive mark of heralds and ambassadors whose persons it rendered inviolable. The Caduceus itself was not used by the Romans but the derivative *Caduceator* occurs in the sense of peace commissioners. This mark therefore has been used from early history as an emblem of authority, law and order, peace and health. Moreover, since the serpents represent sagacity, underground mysterious knowledge, health and victory over diseases, the rod, the wings and the serpents have been recognized by the medical profession as the honourable emblem of sanctity, purity and health from the earliest knowledge of healing to the present day all over the world by the modern medical profession. Figure 7, plate XXXII, gives the representation of the original sign of Caduceus. It represents the rod of Mercury, the wings towards the top of the rod and two serpents coiling around the rod. Different medical societies have introduced slight modifications in the above emblem but in all the cases the rod and the serpents remain constant theme of the emblem.

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PLATE XXXI

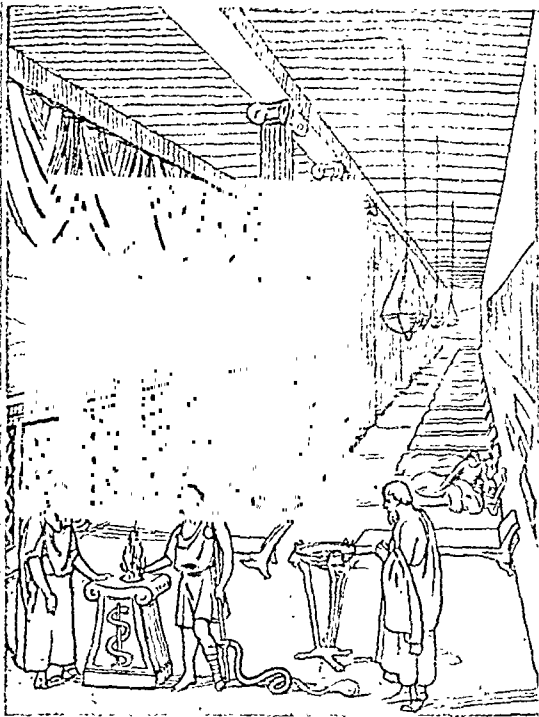
NEUROMYELITIS OPTICA (DEVIC'S DISEASE) : NAUMANN T MASCATI. (O. A.) PAGE 533



Fig. 1.—Photograph of patient just after pyrexia. Notice left leg which is affected.



Fig. 2.—Photograph of patient learning to stand up without support after 3 intraspinal injections.



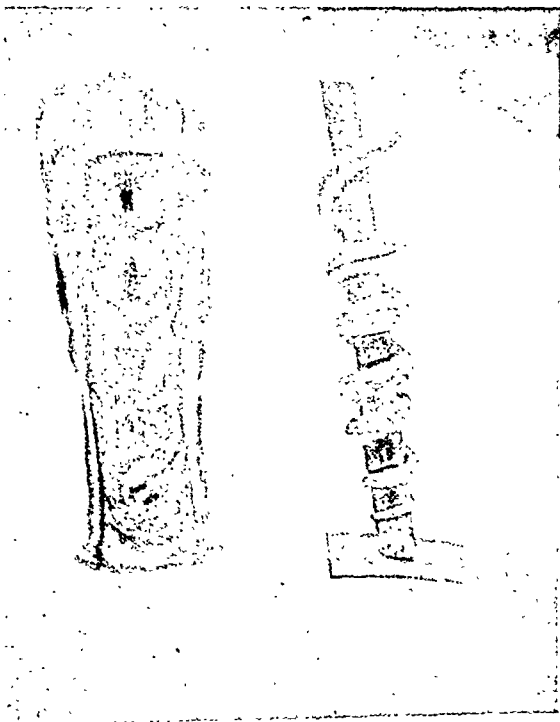
1.—After Dr. Caton's Temples and of Asklepios at Epidaurus. From Centuries of Health and Physick, p. 56.



2.—The faith healing aspect of serpents in Greek medicine.



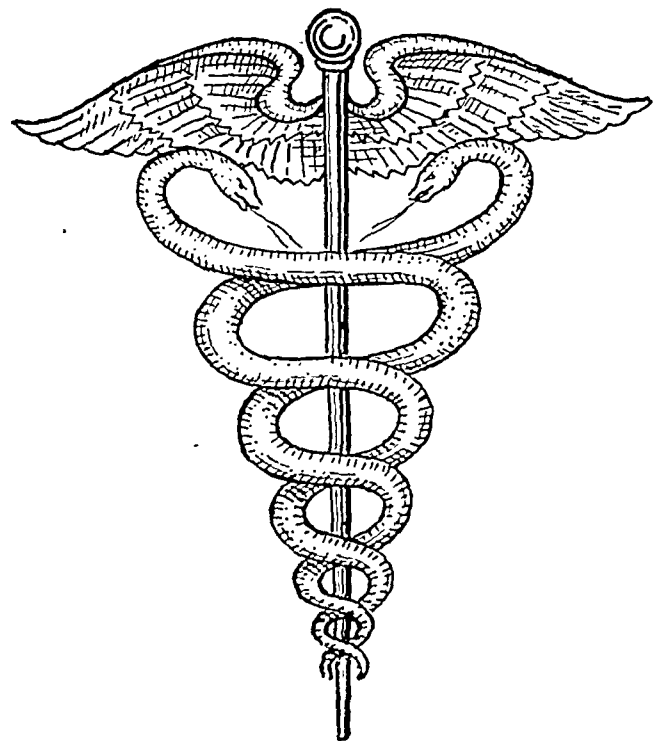
Fig. 3.—Aesculapius sitting on a throne with his daughter Hygieia. A snake is coiling underneath the throne.



s. 4 and 5.—Type of serpents associated with Asklepios and the emblem of Caduceus.



Fig. 6.—Symbol of death and cancer and the timely medical aid by the medical sciences.



CADUCEUS

Fig. 7.—The emblem of the medical profession and the art of healing.

AEROPLANE ACCIDENT IN CALCUTTA

A propeller enters Editor's room

On the 16th November, 1949, at 6 minutes to ten in the morning two aeroplanes collided in mid-air over Calcutta and crashed. One of them crashed into the Calcutta Medical College compound, damaging several rooms in the north-eastern corner of the Calcutta School of Tropical Medicine. The following photographs show the damage done to room No. 17 in which the editorial office is situated. Fortunately none of the staff was hurt.



Fig. 1.—Damage to the window in the eastern wall adjacent to the Editor's seat.

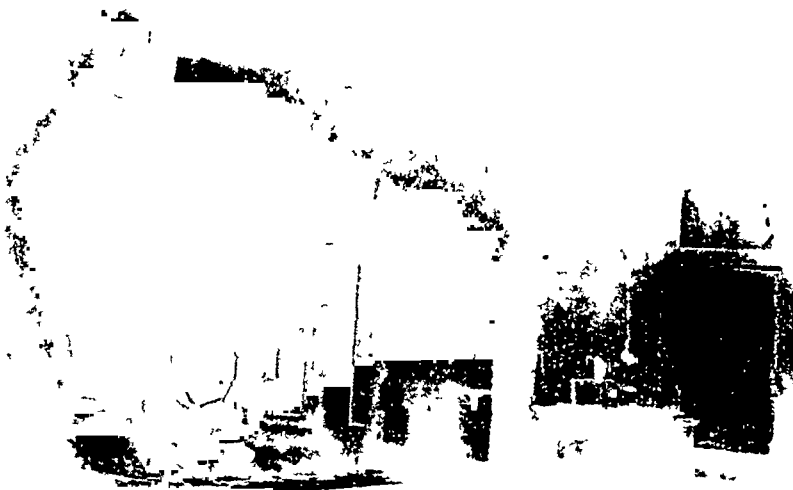


Fig. 2.—Damage to a three-panel window on the northern wall and to another single-panel window on the eastern wall.

PLATE XXXIV

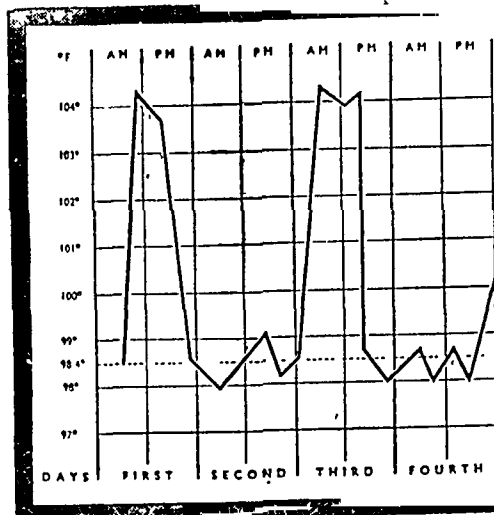


Fig. 3.—Hit and crack in the ceiling by the propeller which entered through the first panel of the three-panel window.



Fig. 4.—The propeller as it finally lay after smashing one chair to pieces and penetrating a wooden fixture.

IN

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- 2 In cardiac cases with pulmonary œdema, or where this is feared, although general œdema may be absent.
- 3 In cases of ascites or anasarca due to hepatic cirrhosis where the renal impairment is not marked.

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Indian Medical Gazette

DECEMBER

POLIO-CONSCIOUSNESS

IN our country organic diseases of the nervous system do not thrive (Greval, 1946). They are, of course, represented as a minority community amongst diseases and deserve all the considerations given to the minority communities in general. Occasionally they carry off victims with horrifying speed and what little could be done is left undone because of a lack of familiarity with the disease concerned. Hence the need for polio-consciousness at the present moment.

Recently we have received communications from our readers on cases of: (1) Encephalitis lethargica (Kundu, 1949; Bhat, 1949). Cases of this disease do occur occasionally and singly. They may occur in bunches too; but a family incidence is suggestive of polio in view of the recent reports on the increased infectivity of the disease. Besides, paralysis and paresis are included in the clinical picture and again polio is suggested. The disease at least deserves a consideration in the differential diagnosis. (2) Rabies after treatment (Garg, 1949; Hatangdi, 1949). That the anti-rabies treatment fails in a very small percentage of cases treated is known. That a paralysis caused by the treatment itself occurs is also known (Greval, 1936). The paralysis may even kill occasionally. In view of the widespread incidence of polio, however, the latter again deserves a consideration in the differential diagnosis. (3) Cryptogenic rabies. Two cases have been described and three more mentioned (Deshmukh, 1949). In this bunch of cases of rabies occurring without a dog bite or indeed bite from any animal known to carry rabies, the polio must be considered and excluded definitely before rabies can be made a water-borne disease. before rabies can be made a water-borne disease as has been suggested.

All this has happened between January and December 1949. This period is also the polio period. We are inclined to pay more attention to a single common disease rather than consider three diseases, specially when they do not conform to the usual clinical picture.

We have recently written on polio (Editorial, 1949) and take this opportunity of emphasizing the following: (1) There is an epidemic type of the disease characterized by influenza-like symptoms, high mortality, muscular spasm and hyperaesthesia of the skin. (2) There is a change in the age incidence. The incidence has

increased in the age group over 16 and decreased in the age group up to 5. (3) There are contact cases and multiple cases in one house. They point to the increased infectivity of the disease. (4) In an epidemic early cases are more severe. (5) Children are more susceptible immediately after tonsillectomy. Operation on nose, throat and teeth are contraindicated during an epidemic. (6) There are three stages in the disease constituting (i) minor illness or abortive polio, affecting the respiratory tract or gastrointestinal tract, 'cold' of the tracts; (ii) pre-paralytic polio, causing the usual aches and pains, stiffness of the muscles of the limbs and back; and (iii) paralytic polio in which paresis is present. (7) The C.S.F. does not give much information. (8) The Kenny treatment with a respirator if necessary and with prophylactic penicillin to guard against infection of lungs is in vogue. (Cases needing respirator do not do well on the whole even after their discharge from the appliance.) Oxygen is used in addition to the respirator. Feeding should be rectal or subcutaneous. Bulbar paralysis is the dreaded involvement. Chemotherapy has been disappointing. (9) In prognosis concerning residual paralysis electric reactions give useful information. (10) The virus consists of a composite group, the Lansing type. It may be derived from natural reservoirs like moles. Animals have been protected against the virus by a vaccine made from inactivated virus. Probably the same method of protection will succeed in man. Hedgehogs and peaches have been suspected recently. (11) Prophylaxis has failed singularly in polio so far. The disease does not appear to be linked with insanitation at all. (12) The Nicobar epidemic of 1947 may throw some light on the flaring up of the disease within the last three years and its increasing incidence in India. It does not appear to have been studied intensively. (13) The adverse tellural influence on the virus in India will have been established when the crippled cases remain a minor problem after the wave of the epidemic has passed away. So far they have been only a minor problem.

Attention has been called to the meningeal and encephalitic form of the disease (Wechsler, 1947). Belief against multiple clinical form has also been expressed (Walshe, 1947). We prefer the view expressed in the call to attention. It is a sound practice to trace many closely allied manifestations of morbidity to a single central process.

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Snake Bite in India

It would be of great value if a simple test could be devised, whereby it would be possible to diagnose the type of snake which has bitten a victim and, in particular, to differentiate between the bite of a poisonous and non-poisonous snake. Where the snake has been killed and brought for inspection, this is a comparatively simple matter.* Unfortunately, it is only rarely that the body of the snake is produced for inspection. Accordingly, the medical man has to diagnose the case on signs and symptoms alone. A history of snake bite is available. Krait and cobra bites are fairly easy to diagnose—though difficult to distinguish between. There is at first pain at the site of the wound which later gives place to a feeling of numbness and signs of 'intoxication', such as thick speech and unsteady gait. These are followed by marked inco-ordination, ptosis, drowsiness, salivation, respiratory distress and finally, in fatal cases, respiratory failure. In addition, krait bite is often accompanied by colicky pains and diarrhoea. With viper bite the picture is entirely different. Except for prominent fang marks and burning pain at the site of the bite, signs and symptoms may be absent, until hæmorrhages set in or the patient suddenly collapses. A useful sign, not sufficiently appreciated, is the lessened coagulability of the blood. Thus, if the patient comes for treatment more than half an hour after being bitten, one can almost certainly rule out viper bite if the blood coagulates in less than 10 minutes. In the absence of neurotoxic symptoms, this simple test is of great help to exclude the bite of a poisonous snake, in India. We have recently discharged without treatment a number of cases of snake bite so tested. One case, undiagnosable by symptoms, showed delayed coagulation and antivenene was thereupon administered. This patient was almost certainly bitten by a viper, as his blood, 12 hours after treatment, was still incoagulable. Antivenene saved this patient's life and no further symptoms developed, with the exception of a slight rise in temperature.

* A reference to Prater's chart, published under the auspices of the Bombay Natural History Society, will readily enable the practitioner in India to identify the snake, if poisonous. This excellent chart should be kept in every dispensary in India.

A chart from the *Field Service Hygiene Notes*, 1945, reproduced in the tenth edition of Lyon's *Medical Jurisprudence for India*, is also useful.—S. D. S. G.

Hæmorrhages did not occur, despite the greatly reduced coagulability of the blood.

Indian viperine venoms are powerful blood coagulants. Within a few minutes of the injection of Russell's viper venom into animals, the clotting time of blood is markedly decreased. At this stage fibrin is being rapidly deposited in capillaries. Later, as the blood becomes more and more defibrinated, the clotting time becomes more prolonged, till finally the blood may be rendered completely incoagulable. At this stage hæmorrhages are liable to occur. These hæmorrhages are not due to any special 'hæmorrhagin' moiety or any 'antifibrin ferment' contained in this venom but are essentially the end-results of the action of its powerful coagulant fraction. It follows that in the treatment of viper bite, if the case is seen at an early stage and if specific antivenom serum is not available, anti-coagulant therapy, such as the use of heparin, may be of very great value. Experimentally it has been shown that heparin effectively neutralizes *in vivo* and *in vitro* the coagulant effect of the venom of Russell's viper and to a somewhat less extent that of *Echis carinata* and many other viperine snakes (Ahuja *et al.*, 1947, 1948a, 1948b). It follows that the treatment of viperine poisoning by the administration of blood coagulants, as is normally practised, is irrational, especially in the early stages.

The great majority of snake bites occur in rural areas, for snakes in villages are more plentiful than in towns, and the barefooted villager working in the field is more exposed to the risk of snake bite. This is doubly unfortunate as it is not possible to stock antivenene in many village dispensaries, for not only would this procedure necessitate the immunization of thousands of horses annually for the production of serum, but the serum, improperly stored in village dispensaries, would soon deteriorate. The need for a readily procurable, cheap substitute for antivenene is therefore great. Unfortunately, no such substitute is available. Soap solution is, however, worthy of trial. A 5 per cent watery solution of carbolic soap should be stocked in village dispensaries, ready for use, and in case of cobra or krait bite, the bitten area should be infiltrated with the solution without delay. In experimental studies, this method of treatment has proved effective against the venoms of Indian and South African cobra (*Naja naja* and *Naja flava*), krait (*Bungarus caruius*) and ring hals (*Sepedon hamachates*), provided the soap solution is so injected as to come into direct contact with the unabsorbed venom (Ahuja and Brooks, 1945, 1948; Christensen and Waal, 1947). This is not always a simple matter, for in such experiments, especially when carried out on pigeons and guinea-pigs, the operator must take great care to infiltrate the envenomed area. In two such experiments on pigeons, using the same

dosage of venom, with the same time interval between the injection of venom and commencement of treatment and the same solutions of soap and venom, one operator saved 8 out of 9 pigeons while another operator saved only 1 out of 9.

Soap would appear to act by delaying absorption of these venoms (krait and cobra) so that even when life is not saved the death period is considerably prolonged. Advantage may be taken of this in villages where the soap should be given as a first-aid treatment and the patient then transported, as quickly as possible, to the nearest town for specific treatment. As the union of cobra venom with the cells of the central nervous system is fairly loose, treatment with antivenene, even in advanced cases of cobra poisoning, may prove effective.

Soap solution is useless for viper bite; it cannot take the place of specific treatment; it should on no account be given by the intravenous route; and it may give rise to ulceration though, in experimental animals such as pigeons, rabbits and sheep given 1 cc. to 5 cc. quantities of soap solution, this has been found to occur only exceptionally. This must, however, be weighed against the fact that the life of the animal can be saved at the price of a 'local ulcer' if it occurs.

What the detoxifying action of soap is attributable to is not known but this much is certain that it is not due to the alkali present. Tests carried out with alkali of the same concentration as is present in soap have shown no effect in the detoxification of venom. It is possible that it may be due to the depressant action of soap on surface tension and that the tension at the venom-soap interface may not be the same for all venoms. This might explain the different results obtained with different venoms when acted upon by the same soap. Further work is indicated on the detoxifying action of venoms of pure soaps prepared from various members of the fatty acid series. The fact remains, however, that soap can detoxify some types of venom, and in the many borderline cases in which just sufficient venom has been injected by the biting cobra or krait, soap promptly infiltrated is likely to tip the scales in favour of the patient and this treatment alone may, therefore, prove effective in many cases.

M. L. A.

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Medical News

TYPHUS EPIDEMIC IN AFGHANISTAN

(Abstracted from *The Medical Officer*, No. 2141, Vol. LXXXII, No. 6, Saturday, 6th August, 1949, page 59)

News of the outbreak of a louse-borne typhus epidemic in Afghanistan has been received at the Geneva headquarters of the World Health Organization. Steps already have been undertaken to render international aid to the stricken country. The Afghan Minister of Health, reporting the outbreak to the W.H.O. regional office in New Delhi, asked for assistance in the form of vaccine and DDT insecticide. Recent outbreaks of typhus epidemics, such as occurred in Roumania in 1948 and in North Africa in 1942, were quickly brought under control by the widespread use of DDT in powder form, as well as vaccination. Threatened populations are freed of lice by squirting DDT powder under their clothing. This method was first used in Naples, in 1943, on a large scale, when the allied armies, upon entering the city, discovered cases of typhus.

THE 6TH INTERNATIONAL CONGRESS OF RADIOLOGY, LONDON, 23RD TO 29TH JULY, 1950, AND THE INTERNATIONAL ANATOMICAL CONGRESS, OXFORD, 25TH TO 28TH JULY, 1950

THE 6th International Congress of Radiology will be held in London from 23rd to 29th July, 1950. The headquarters will be the Central Hall, Westminster, and meetings will also take place at the Church House and Caxton Hall. In addition there will be a Scientific Exhibition at the Central Hall, and a Technical Exhibition of apparatus in the Halls of the Royal Horticultural Society.

Those wishing to attend the Congress as Full Members (£7 7s.), or as Junior Members (under 30 years of age on 1st January, 1950—£4 4s.) must be members of a radiological society or sponsored by a radiological society.

Application should be made by form. Forms and information may be obtained from:—

The Secretary,
 The 6th International Congress of Radiology,
 45, Lincoln's Inn Fields,
 London, W.C.2.

From this address you should be able to obtain details regarding travel arrangements, demonstrations to take place in the radiological departments of London hospitals, the submission of papers and exhibits, and the programme of tours to centres of interest in Great Britain.

The International Anatomical Congress will take place at Oxford from 25th to 28th July, 1950. Application for membership should be made by form. Application forms, and information regarding travel arrangements, programme, and accommodation can be obtained from:—

The Congress Organiser,
 International Anatomical Congress, 1950,
 Department of Human Anatomy,
 University Museum,
 Oxford.

EXTENSIVE ACTIVITIES OF SYDNEY DENTAL HOSPITAL

(Reproduced from Release No. P./1321 issued by the Public Relations Officer, Australian High Commissioner's Office, New Delhi)

SYDNEY DENTAL HOSPITAL, set up in 1939, is the largest and one of the most modern dental clinics in the British Commonwealth.

More than 60,000 patients a year are treated in the eight-story building which also houses the Sydney University Dental Science Faculty School.

But general dental work is only part of the many activities of the hospital—a Sydney landmark with its exterior walls mostly of glass to let in more natural light.

It also conducts the Dental Research Institute, two travelling rail clinics, special clinics for children and pre-school clinics at day nurseries and kindergartens; a special section for expectant mothers; a plastic surgery section where artificial ears, noses, eyes and facial moulds are made.

The Dental Research Institute is the leading organization of its kind in Australia. Directed by Dr. N. E. Goldsworthy, the staff includes many first-grade diagnosticians, scientists and technicians. Main research interest at present is the study of dental decay and its causes.

The rail clinics are a complete surgery and repair room on wheels and may be taken to any point served by New South Wales, 6,128 miles of rail network.

Each of these clinics is staffed by two dentists, two nurses and two mechanics. They do all types of dental work free of charge.

The primary aim is to cater for old age and invalid pensioners and anyone getting any form of Government social service assistance—people who could not otherwise afford dental treatment and who could not travel to the Sydney Dental Hospital. They sometimes spend up to six months in some rural areas.

The forthcoming arrival of a rail clinic car is well advertised in all the country towns and every pensioner is advised by mail to visit the clinic if he requires dental attention.

Many of the children's clinics at the day nurseries and kindergartens are designed and furnished specially. All of them are staffed by operators used to children. They are an important factor in overcoming the dentist bogey and making young children and their parents' dental care conscious.

At their special section, mothers-to-be can obtain advice about diet and receive attention they may need before the birth of their child.

In co-operation with plastic surgeons, artificial ears, noses, eyes and facial moulds are made for needy patients at a nominal charge.

There are now 770 dental students, more than 200 of them women, at the Sydney Dental School. Many of the students are former servicemen and women.



LONDON NURSING EXHIBITION

The 34th Annual London Nursing Exhibition was held recently at Seymour Hall, London, in conjunction with the Annual Professional Nurses and Midwives Conference. Sir Cecil Wakely, President of the Royal College of Surgeons, watching a demonstration by Mr. G. W. Wells, a member of the staff of the Atomic Energy Research Establishment, Harwell, of a 'Geiger Counter', the latest development of modern science for the diagnosis of thyroid gland disorders. The patient drinks an iodine solution that has previously been made radio-active by insertion in an Atomic Pile. The result of the subsequent count enables a diagnosis to be made of the condition of the thyroid gland.

THE INTERNATIONAL AND FOURTH AMERICAN CONGRESS ON OBSTETRICS AND GYNÆCOLOGY. 14TH TO 19TH MAY, 1950, HOTEL STATLER, NEW YORK

THE Chairman of the General Programme Committee for the forthcoming Congress is Dr. Howard C. Taylor, Jr., of New York City. To date the following speakers have been placed on the programme by Doctor Taylor and assigned the designated subjects. Each paper will be about twenty-five minutes in length and will be followed by a formal discussion.

Professor Heinrich Martius of the Department of Obstetrics and Gynæcology of the University of Goettingen in Germany will speak on the general topic: Radiation Techniques and Results in the Treatment of Cancer of the Cervix.

Dr. Leon Gerin-Lajoie of the University of Montreal will speak on utero-salpingography as a means of differential diagnosis in hæmorrhages of the uterus.

Dr. Charles D. Guerrero of Mexico City will present an address based on the use, misuse and abuse of surgery in gynæcology.

Dr. Arthur T. Hertig of the Harvard Medical College will address the Congress on 'Implantation of the Human Ovum'.

Dr. Carl Kaufmann, Professor of Obstetrics and Gynæcology of the Faculty of Medicine at Phillip University at Marburg in Germany, will speak on the subject of the relations of endocrinology to gynæcology.

Dr. Hans Ludvig Kottmeier of the Gynæcological Department of the Radio-pathology Institute in Stockholm, Sweden, will lecture on various aspects of cancer therapy.

Dr. Lakshmanaswami Mudaliar of Madras University in Madras, India, will speak on a topic related to the toxæmias of pregnancy.

Dr. Manuel Luis Perez of Buenos Aires has taken as his subject: 'The Usefulness of Antibiotics in Obstetric Surgery'.

Dr. S. R. M. Reynolds, Ph.D., of the Department of Embryology at the Carnegie Institute in Washington, D. C., will speak on: 'The Contractility of the Human Uterus and Its Physiological Basis'.

Dr. Walter Seegers of the Department of Physiology of Wayne University College of Medicine in Detroit will talk on the work done by him and Dr. Charles Schneider on the fundamental aspects of the blood clotting problem and the practical aspects of the problem in obstetrics.

Dr. Harold H. Sheehan, Professor of Pathology at the School of Medicine of the University of Liverpool in England, will speak on the kidney in abruptio placentæ.

Dr. Jean Snoek of the Hospital St. Pierre at the University of Brussels has for his subject: 'Some Aspects of the Renal Function in Pregnancy and Their Morbid Consequences'.

Dr. Herbert F. Traut of the University of California Medical School will speak on the early diagnosis of uterine cancer.

The above speakers are all to appear during the five morning general sessions of the programme and the list is but partially completed. Other noted men will take part in the afternoon programmes of the medical section of the Congress being arranged by a sub-committee headed by Dr. Newell Philpott of Montreal. Separate afternoon programmes are being arranged for nurses by Miss Margaret A. Losty, R.N., of New York, for public health people by Dr. Edwin F. Daily of Washington and for hospital administrators by Dr. G. Otis Whitecotton of Alameda. Doctor Daily is also arranging the programme of speakers on the economic aspects of obstetrics and gynæcology that will occupy Wednesday morning. The Wednesday

afternoon programme will be entirely planned and presented by the National Federation of Obstetric-Gynæcologic Societies. For registration details, housing data and other aspects of the Congress address inquiries to Dr. Fred L. Adair at 161 East Erie Street, Chicago 11, Illinois.

(See also *Indian Medical Gazette*, June 1949, p. 262.—*Edron, I.M.G.*)

V.D. CONTROL IN S.E. ASIA

(The following was received in New Delhi from W.H.O. Headquarters in Geneva)

(Reproduced from Press Release No. SEA/PR/14 issued by Regional Office for S.E. Asia, W.H.O., New Delhi)

ONE of the venereal disease control projects recommended in the report of Dr. George Leiby, W.H.O. consultant in V.D., who recently spent several weeks in India on the Government's invitation, is the development of a provisional V.D. Control training centre for India.

The training centre is planned to be in Simla where a W.H.O. V.D. Control team has been operating since the summer and has established a diagnostic laboratory along the most modern lines. It is proposed that the centre will train doctors, laboratory technicians, nurses and public health workers in the latest advances in methods of control of syphilis and other venereal infections. The existing W.H.O. team in Simla, it is stated, is already able to accept a limited number of trainees.

Under an agreement being negotiated by the Government of India with the U.N. International Children's Emergency Fund (U.N.I.C.E.F.), doctors completing a course at the W.H.O. Simla Centre will be equipped by U.N.I.C.E.F. with indispensable medical supplies for the application of new techniques. At present V.D. control supplies and equipment, and especially penicillin, laboratory, diagnostic and educational material, are often difficult to get.

Ceylon has also expressed great interest in W.H.O.'s V.D. control plans. Dr. Leiby, who is professor of Internal Medicine and Syphilology at the University of California at Los Angeles, gave several lectures in Colombo on modern treatment methods, attended by over 600 doctors, public health officials and medical students.

It is believed that adequate V.D. services can be introduced in Ceylon in conjunction with the excellent Mother and Child Welfare Organization already existing there. On the basis of data furnished by Dr. Leiby, the experts of the W.H.O. V.D. demonstration teams, and the surgeon in charge of V.D. control in Ceylon, the Ceylon Department of Medical and Sanitary Services have already issued a publication 'Modern Concepts of Syphilis Control'. One injection of 300,000 units of procaine penicillin G with aluminium monostearate, the experts agree, is sufficient treatment for the majority of cases of early syphilis.

Among other V.D. control plans being drafted by W.H.O. in S.E. Asian countries is a yaws eradication project in Indonesia, with the help of U.N.I.C.E.F. which has allocated 700,000 dollars to this project. Yaws, a syphilis-like disease, non-venereally transmitted, is especially prevalent among children (up to 75 per cent); it incapacitates an important proportion of the rural population in many tropical areas, and has a deteriorating effect on agricultural productivity and development.

The yaws eradication project in Indonesia would be combined with a syphilis control programme, since penicillin is the therapeutic agent employed for both diseases.

Dr. Leiby is at present visiting Rangoon and Bangkok to work out V.D. control measures in consultation with the Burmese and Thai Governments. After making a final report to W.H.O. he will return to the United States.

Dr. N. Jungalwalla, it is announced, will shortly take up his post as permanent V.D. adviser to the W.H.O. Regional Office in South East Asia. Dr. Jungalwalla was a member of the W.H.O. Study Commission on V.D. which recently toured the United States.

MEDICAL LITERATURE AND TEACHING EQUIPMENT FOR S.E. ASIAN COUNTRIES

(Reproduced from Press Release No. SEA/PR/17 issued by W.H.O. Regional Office for S.E. Asia, New Delhi)

TEN THOUSAND DOLLARS has been allotted as Burma's share of \$24,000 which has been made available by the World Health Organization to meet urgent requirements of five S.E. Asian countries in medical literature and teaching equipment, according to information just received in New Delhi from W.H.O. Geneva Headquarters. It is understood that the most pressing needs of the Pasteur Institute, the Medical College, and the General Hospital in Rangoon will be partly met from this allocation from the 1949 Budget of W.H.O.

Burmese hospital and nursing staff and medical students have been working under terrible handicaps resulting from the pillage and destruction of books and instruments during the war, reported a W.H.O. official who visited Rangoon in the summer.

India's share in the 1949 W.H.O. programme of supply of medical literature and teaching equipment will be \$8,500. It is announced that this will be used to provide equipment needed to strengthen the Malaria Institute in Delhi.

Thailand has been allotted \$3,000 and Ceylon \$1,000 to help meet the most urgent of their requirements under the programme. Both countries have sent full particulars to W.H.O. of textbooks and equipment needed.

The remaining \$1,500 will go to Afghanistan where, it is learned, it will probably be used to supply laboratory equipment needed by the Kabul Institute of Public Health and Hygiene, and for medical literature.

The Medical Literature and Teaching Equipment Programme of W.H.O. provides for the supply of material not obtainable locally in national currency, in cases where real need can be demonstrated. The aims of the programme, as officially stated, are:—

- (i) To replace material which has been destroyed by war;
- (ii) To rehabilitate inadequate and outdated libraries and teaching laboratories; and
- (iii) To furnish a nucleus of textbooks and teaching equipment where especially needed to raise standards of medical education.

W.H.O. expects to double the total volume of its services in this field in 1950.

DOCTOR RAJAM ELECTED VICE-CHAIRMAN OF INTERNATIONAL V.D. EXPERT GROUP

(Reproduced from Press Release No. SEA/PR/9 issued by W.H.O. Regional Office for S.E. Asia, New Delhi)

DR. R. V. RAJAM, M.B., M.S., M.R.C.P., Principal and Professor of Venereal Disease at the Madras Medical College, was elected Vice-Chairman of the W.H.O. Expert Committee on Venereal Diseases, meeting last week

in Washington, U.S.A., with V.D. experts from 12 countries attending, according to information just received at the W.H.O. Regional Office here. A venereal disease control demonstration campaign, the Committee learnt, had been started last May in the Himachal Pradesh, India, by the first W.H.O. V.D. Team ever to be put into the field.

Stressing the importance of fundamental health education of the public in relation to venereal disease infections, the experts were of the opinion that it would be useless to shrink the reservoirs of venereal disease unless something was done to change the fundamental attitudes of people generally towards V.D. It was recommended that W.H.O. demonstration teams like that now operating in India could use definite areas as starting points for co-operative health education programmes with the health departments of local authorities and community groups. New techniques could be established and better methods developed within the cultural pattern, religious codes and social organization of each demonstration area.

Considering the maritime aspects of V.D. control, the Committee recommended free treatment for seamen of all nationalities, and notification by physicians and medical institutions of cases of V.D. to health administrations for statistical purposes. Another recommendation was the establishment of local venereal disease commissions similar to the one already sponsored by W.H.O. in the Rhine River area in Europe, and the launching of V.D. control demonstration projects in ports in S.E. Asia and the Eastern Mediterranean under the expanded W.H.O. programme for 1950 and 1951.

The expert went on to discuss the wider problem of treponematoses and the biological interrelationship of syphilis, yaws, pinta and bejel. Yaws and bejel are diseases having some clinical resemblance to syphilis but are non-sexually transmitted and occur principally among children. The Committee felt that a correlated study bearing on the interrelationship of the causative agents of these diseases was an essential undertaking. It further recommended that immunity relationships in treponematoses be studied in a co-operative laboratory investigation scheme. Material for this study could be obtained from the W.H.O. V.D. units in South East Asia, in the Eastern Mediterranean region and elsewhere.

CHOLERA CONTROL PROJECT IN MADRAS PROVINCE RECOMMENDED BY INTERNATIONAL EXPERT GROUP

(Reproduced from Press Release No. SEA/PR/13 issued by W.H.O. Regional Office for S.E. Asia, New Delhi)

ACTIVE field work in cholera control aiming at developing techniques for the ultimate stamping out of this terrible disease will be begun next year by a W.H.O. Cholera Control Team in the Cauvery Delta region of Madras Province where the population suffers the ravages of cholera all the year round, according to plans worked out by the international cholera experts attending the Third Session of the Joint Study Group on Cholera of the Office International d'Hygiene Publique and the World Health Organization which terminated to-day in New Delhi. The Group also recommended the establishment of a second W.H.O. Cholera Control Team in a similar deltaic region in the East Bengal Province of Pakistan, and laid down the lines of further research to be undertaken into the factors responsible for the persistence of cholera outside the 'cholera season' in so-called endemic areas. The meeting of the Joint Study Group on Cholera, which opened yesterday at the W.H.O. Regional Office here, was presided by Dr. C. G. Pandit, Secretary of the Indian Research Fund Association, and formerly Director of the King Institute, Madras.

The experts were unanimous in praising certain investigations into the endemicity, or persistent presence, of cholera at present being carried out by the Indian Research Fund Association (I. R. F. A.), following suggestions made by the Second Session of the Joint Cholera Study Group in Paris last year. Earlier this month, while visiting the Tanjore District in the Cauvery Delta where some of the I. R. F. A. field investigations are being carried on, the Group was able to see cholera patients in their homes and discuss local difficulties. They were impressed by the co-operation forthcoming from the population of the area and their desire to improve their sanitary conditions. The experts also visited laboratories and hospitals in Bombay, Madras, Tiruchirappalli, Dacca and Calcutta. Later they attended meetings of the Cholera Advisory Committee of the I. R. F. A. in New Delhi from 15th to 17th November.

The establishment of one or more W.H.O. Cholera Control Teams in endemic areas was envisaged by the Second World Health Assembly meeting in Rome last June. In working out concrete recommendations concerning sites and methods of work for these teams, the Cholera Study Group laid special emphasis upon the provision of an abundant supply of controlled water, the development of economical and effective excreta disposal methods for individual families, and the health education of the local population to ensure their willing co-operation in the project.

After comparison of reports of studies undertaken in different districts where cholera seems to be constantly present, the Group noted that such endemic areas occurred most frequently in river deltas with high population density and high humidity and where there was abundance of uncontrolled water supplies with high organic content and some salinity. Both the Cauvery Delta in Madras Province and the Ganges Delta in East Bengal conform to this pattern.

Among the problems of cholera endemicity into which the Group recommended that further investigations should be made were the possibility of cholera infection being carried by fish from one place to another, and the part played in the dissemination of the disease by sub-clinical (mild) cases, contacts and convalescents.

The experts reiterated their opinion that cholera immunization was of value as a quarantine measure provided that the vaccine and the mode of vaccination conformed to standards laid down by W.H.O. They also recommended that research should be carried out on the immunity of the population in endemic areas.

A standard method for the laboratory diagnosis of cholera based on recent research work carried out by four Indian scientists was formally approved by the Study Group.

The recommendations of the Joint Cholera Study Group will be submitted to the W.H.O. Expert Committee on Epidemiology and Quarantine which meets next month in Geneva.

Attending the meeting were :

Dr. C. G. Pandit, Secretary, Indian Research Fund Association (Chairman).

Medecin-General M. Vauzel, Director, Public Health Department, Ministry for French Overseas Territories, Paris.

Lieut.-Colonel M. Jaffar, Director-General of Health, Government of Pakistan, Karachi.

Dr. M. Gaud, Director of the Office International d'Hygiene Publique, Paris.

Dr. P. M. Kaul, in charge of cholera studies, W.H.O., Geneva.

Sir Aly T. Shousha Pasha, Director, W.H.O. Regional Office for Eastern Mediterranean.

Dr. C. Mani, W.H.O. Regional Director for S.E. Asia.

Dr. R. Pollitzer, W.H.O. Epidemiologist.

BUFFALO-CATTLE HYBRID DEVELOPED FOR CANADIAN NORTHLANDS

(Reproduced from U.N.E.S.C.O. Features No. 8, 1st November, 1919, p. 17)

A new type of animal has been developed after 25 years' experimentation by the Canadian Department of Agriculture which may eventually make Canada's vast northland self-sustaining in meat production.

The 'cattalo', a hybrid of the buffalo and the domestic cow, is hailed as the answer to the problem of finding an animal to stand up against a northern winter. This new crossbreed is as adept as the buffalo at foraging for food through heavy snow and, at the same time, is as disease-resistant as ordinary cattle.

INDIAN ASSOCIATION OF PATHOLOGISTS

THE Indian Association of Pathologists was inaugurated at the Lady Hardinge Medical College, New Delhi, in November 1949. About 30 pathologists from all parts of India attended the inaugural meeting in which the constitution of the Association was adopted and the following office bearers were elected for the year 1949-50—

President—V. R. Khanolkar.

Secretary—P. N. Wahi.

Joint Secretary—G. L. Sharma.

Treasurer—H. Patil.

FIGHT AGAINST TROPICAL DISEASES

VICTORY OVER MALARIA IN SIGHT

By SIR PHILIP MANSON-BAHR

Well-known British Consulting Physician in Tropical Diseases

(Reproduced from Release No. B.F. 2324 issued by British Information Services, New Delhi)

MALARIA, sleeping sickness, yellow fever—these are but a few of the many dread diseases against which British scientists and doctors have been waging a ceaseless war.

In this special article, an expert on tropical diseases reviews what has already been achieved. The work of British pioneers has brought health, prosperity and happiness to millions of people throughout the world.

Britain is waging an unceasing war in the tropics not only against the diseases which are peculiar to warm climates, but also against that whole array of scourges which afflict mankind.

Malaria, sleeping sickness, yellow fever: the list is a long one. The most common of tropical diseases is, however, malaria, constituting until recently the chief bar to progress and development. But now it can be claimed that it has been to a great extent arrested and that ultimate victory is in sight.

Let us consider how this transformation has been achieved.

INTENSIVE STUDIES

When some 50 years ago the mosquito-transmission of malaria had been proved beyond doubt, its eradication at that time appeared comparatively simple. It spelt, in fact, the destruction of mosquitoes wherever malaria was rife, though it soon had to be accepted that this was an impossible task.

As the result of intensive studies by entomologists in many lands, it became evident that for some biological

reasons only a comparatively small number of anopheline mosquitoes are capable of transmitting malaria from man to man, and that each of these favours certain breeding places and maintains peculiar feeding habits, so that by concentrating attacks upon them, within the limits of their own peculiar haunts, some success might be obtained. This method was aptly termed 'species sanitation'.

The operative procedures entailed in carrying out these measures differed widely in different countries. In Malaya, for example, some species have been to a great extent eliminated by altering the environment of their breeding waters. Some are partial to shade and concealment; others court the sunlight, and so on. At the present time anti-malarial campaigns have been completely revolutionized by the application of D.D.T., an insecticide which has proved itself to be the most efficient weapon yet discovered.

MALARIA IS RECEDING

Throughout the whole of Equatorial Africa, *Anopheles gambiae*, a common as well as the most dangerous carrier of malaria, flourishes in almost every collection of water, however polluted or foul. Until two years ago the possibility of eradication of this small insect from such an immense area appeared fantastic, but now with the example of the successful campaigns in Sudan and Upper Egypt and with the introduction of other insecticides, such as gammexane, malaria is rapidly becoming a rarity.

Malaria, indeed, is receding wherever the spraying of mosquito breeding grounds is being undertaken. It was recently announced that the island of Cyprus has been freed from the menace after a D.D.T. campaign which has served as a model for the world.

In British Guiana, Dr. George Giglioli has been almost equally successful in an even more remarkable feat, but there he had to deal with vast alluvial plains with rice and cane-fields, swamps and waterways stretching for hundreds of miles. The brunt of this attack was directed against the two most dangerous species—*Anopheles darlingi* and *A. aquasalis*—by spraying huts and dwelling houses which they frequented with D.D.T. In spite of the fact that both these dangerous species have entirely different breeding habits—one breeds in fresh water, the other in brackish—within the space of two years they have been brought to the verge of extinction and concurrently malaria has practically disappeared.

SLEEPING SICKNESS

When we turn to trypanosomiasis, or sleeping sickness, there is also a stirring tale to tell. The trypanosome is a small tadpole-like creature which lives in the blood and is transmitted by vicious and blood-thirsty tsetse flies. These insects are confined to Equatorial Africa, and wherever they abound they spell death to man and his domestic animals.

It is estimated that of the 65 million residents of tropical Africa no fewer than 2,000,000 are infected with the deadly trypanosome. On account of this, only two-fifths of the enormous territory of Tanganyika are suitable for settlement and development; the rest is one vast fly-belt. Some 21 species of tsetse are known to science, of which some six are adapted to the conveyance of the germ of sleeping sickness; and it has now been discovered that for each species of fly certain plant associations and climatic conditions are essential in order that it may flourish.

The fight against sleeping sickness has been long and protracted. Whole populations have been transplanted from danger areas, and the ingenuity of many devoted entomologists has been taxed to the utmost to discover methods of controlling the fly. Vast schemes for destroying their breeding places have been put into execution. D.D.T. 'smoke' spread by aircraft has, indeed, achieved some local and temporary success.

Powerful curative drugs, such as antrypol and tryparsamide, have been discovered and freely used; but the battle is not yet won.

The epic of the Anchau corridor has now been told. The market town of Anchau in North Nigeria in the Emirate of Zaria has always constituted a hot-bed of sleeping sickness and, owing to its filthy and insanitary state, a danger to the community. To free this area from sleeping sickness, 700 square miles of country had to be cleared of bush, and, within the space of 10 years, the local population had been resettled in a new town with model wells and market-places. Cattle, pigs and poultry have been introduced, and flourish there. The cesspit which constituted old Anchau has now been transformed into a settlement aptly termed Takalafiya or 'Walk in Health'. For this magnificent achievement Dr. H. M. Lester, Dr. T. A. M. Nash and Dr. Kenneth Morris must be given full and generous credit.

CONQUEST OF YELLOW FEVER

The story of the conquest of yellow fever, or 'yellow jack' as it was known to our forefathers, has been one of constant and heroic endeavour in which British scientists have played a leading part and one in which valuable British lives have been sacrificed. A hundred years ago yellow fever in epidemic form swept across the West Indies and the South American continent and from time to time broke out also in West and Central Africa.

The germ cause has been found to be an ultra-microscopic virus which is present in the blood in the first three days of the fever and is disseminated from the sick to the healthy by a gaily marked 'tiger mosquito'—*Aedes aegypti*. Fortunately this is a domestic insect abounding in the haunts of man, especially in large towns, whence it can be easily ousted by D.D.T. This has now been done in many parts of South America and West Africa, so that with its disappearance yellow fever has been banished from the main centres of population.

With the development of irrigation and cultivation bilharziasis is spreading throughout the Continent of Africa. The bilharzia (so-called after its discoverer, Bilharz—and familiarly nicknamed 'Bill Harris' by British troops) is a worm, just under half-an-inch in length which lives securely within blood vessels. Here the female produces a great number of hard-shelled eggs which are shed outside the body in the excreta and, when passed in water, give rise to a motile ciliated creature which burrows into the liver of certain fresh water snails which abound in streams, ponds, rivers, reservoirs and other collections of water.

In this organ an elaborate reproduction takes place, the final phase of which is the cercaria, a small thread-like creature with a bifid tail which swims actively in water for about two days. This, now a juvenile bilharzia worm, is attracted to man and, by burrowing through the skin, enters the body and settles down within the portal vein. It is obvious that in the extermination of these peculiar snails, which constitute the host of the bilharzia parasite, lies the only hope of curtailing its ravages. This is a gigantic task which entails the draining of streams, ponds and waterways in an unceasing destruction of these molluscs with sulphate of copper.

This brief account is a story of the manner in which the defeat of the main tropical diseases has been, or is being, brought about. It is probably true that, perhaps with the exception of leprosy, we now possess efficient drugs which are antidotes for them all. This is the lynch-pin upon which the health, prosperity and happiness of millions of people depend. For this happy solution a tribute should be paid to members of Britain's Colonial Medical Service, who, unread and unsung, sometimes subjected to unjust and uninformed criticism, have laboured on, often amidst uncongenial surroundings, such as can hardly be realized by many.

NEW DRUG FOR TREATMENT OF PERNICIOUS ANÆMIA

(Reproduced from Release No. B.F. 2325 issued by
British Information Services, New Delhi)

COMMERCIAL production of the new anti-pernicious anæmia drug Cytamen, a vitamin B₁₂ concentrate produced by deep fermentation methods, has been announced by a Middlesex firm. This drug not only restores the supply of red cells in the blood but corrects the nervous disorders and deterioration of the spinal cord caused by this disease.

Commercial production of this drug follows the firm's announcement last May that after 10 years' research they had isolated the pure anti-pernicious anæmia factor—vitamin B₁₂.

Cytamen is more active than any other known vitamin or hormone, while the rich red colour of the crystalline factor is due to the presence in the molecule of an atom of cobalt. It is claimed to be the first time that cobalt has been detected in an isolated substance of natural origin.

AMENDMENTS TO DRUGS RULES, 1915

No. F.18-1/46-D., Government of India, Ministry of Health, New Delhi, the 16th December, 1949.

NOTIFICATION

IN exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendment shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said sections, namely :—

In Schedule B to the said rules, in item I. after the entry 'Adrenaline and preparations of Adrenaline' the following entry shall be inserted :—

'Penicillin . . . Rs. 25.'

(Sd.) J. N. SAKSENA,

Under Secretary.

No. F.1-14/47-D., Government of India, Ministry of Health, New Delhi, the 20th December, 1949.

NOTIFICATION

IN exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendment shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said sections, namely :—

In the said rules—

In the proviso to sub-rule (3) of Rule 96, for the words 'the container' the words, 'any glass container other than ampoules' shall be substituted.

(Sd.) J. N. SAKSENA,

Under Secretary.

No. F.1-44/47-D., Government of India, Ministry of Health, New Delhi, the 21st December, 1949.

NOTIFICATION

IN exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendment shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said sections, namely :—

In paragraph I of Part X of Schedule F to the said rules, for the words 'prepared from the gut or any

tissue of an animal', the words 'of animal, vegetable or synthetic origin' shall be substituted.

(Sd.) J. N. SAKSENA,

Under Secretary.

No. F.1-3/47-D., Government of India, Ministry of Health, New Delhi, the 27th December, 1949.

NOTIFICATION

IN exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendments shall be made in the Drugs Rules, 1915, the same having been previously published as required by the said sections, namely :—

In the said rules—

I. To Rule 46, the following proviso shall be added, namely :—

'Provided that no protocols of tests shall be supplied in the case of patent and proprietary medicines registered at the Central Drugs Laboratory.'

II. In Schedule A in form 13—

(a) before item 7 an asterisk mark shall be inserted, and

(b) the following footnote shall be added at the end, namely :—

'* No protocols of tests applied shall be supplied in respect of patent and proprietary medicines which are registered at the Central Drugs Laboratory.'

(Sd.) J. N. SAKSENA,

Under Secretary.

The Indian Medical Gazette Fifty Years Ago

ENTERIC FEVER AMONG NATIVES OF INDIA

(From the *Indian Medical Gazette*, December 1899, Vol. 34, p. 451)

It may be that some apology is required for again dragging on the scene the well-worn subject of the existence or prevalence of enteric among natives of India. As it happens, however, we have been able to offer to our readers two papers dealing with this subject, one by Major Andrew Buchanan of Nagpur, who has had a considerable experience of enteric fever in native prisoners, in most cases being able to verify the diagnosis by *post-mortem* examinations.

The second paper, in our last issue, by Captain R. H. Maddox, I.M.S., gave a case which it would be difficult, if not impossible, to call other than enteric, though it was not absolutely typical, and though no possible source of any infection could be traced. Our columns in past years have often contained discussions on the subject, but it cannot be said that this question,

one of the utmost importance, is yet finally settled. A review of all that has been written on the subject, and a pretty extensive inquiry as to the views of medical men in India, who are in a position to give an opinion on the subject seems to result in something like the following.

Among those who have great experience of the disease, as it prevails among British soldiers in India, a sometimes half-expressed feeling seems to exist that enteric fever does prevail among natives, but that it is often diagnosed as 'simple continued' or 'remittent fever'. We will further on show the futility of this view. Among another class of officers, and they chiefly in the senior ranks, the view is pretty largely held that enteric fever is very rare or almost unknown among natives; on the other hand, to judge by the reports of younger men, it would appear that enteric fever is by no means so rare in natives as is generally supposed, and this is an opinion shared also by some men in a position to give an authoritative decision on the matter, *e.g.* Major Drury, I.M.S., who, as Professor of Pathology in the Calcutta Medical College, is peculiarly in a position which enables him to give a weighty opinion on the subject. He believes that enteric fever is more common among natives of Bengal than is commonly believed.

The question is not altogether one which can be profitably discussed with reference to natives of India only. In other tropical countries and among other tropical races the same vexed question arises. Our readers may remember that some months ago we called attention to a remarkable article in the *Lancet* in which Dr. Brown gave as his opinion that enteric fever was certainly common among natives of the Malay Peninsula, basing his view on his examinations of their blood by Widal's test. We think, however, that we are correct when we say that this investigation took place in the early days of the use of Widal's test, and before it became certain that it was only in very high dilutions that this test was of value; and we think the same fallacy underlay the experiments made by Major S. J. Freyer, R.A.M.C., a couple of years ago, when he claimed to have shown that the majority of natives of India had had typhoid in their youth. Among the Red Indians of North America typhoid is reported by Woodward and other writers to be common, and an assertion similar to that of Major Freyer has been made about the prevalence of enteric in negroes in the United States; but more recent observations throw much doubt upon these statements. On the other hand, it has been shown that the Arabs of Algeria suffer from typhoid about 100 times less than French soldiers stationed in that country. Among the Chinese it is very doubtful if genuine typhoid cases occur; if they do it is only very rarely. On the other hand, in the late Japan-China War,

131 cases were returned as 'enteric'. In many parts of South Africa enteric has undoubtedly appeared among European troops and colonists, and it is said, but we have seen no details to support the statement, that enteric is common among the Kaffir tribes.

In 1897 several medical officers, in their Annual Regimental Reports, gave cases which they regarded as enteric among sepoys, *e.g.* in the 1/4th Goorkhas, the 44th Goorkhas, in the 27th Punjab Infantry at Kila Drosh in Chitral, and in the 4th Punjab Infantry at Wano. The clinical histories in some cases pointed clearly to enteric; in others the reporters state that, if such a heading was permitted, they would have returned them as 'typho-malaria'. Unfortunately, moreover, out of forty-seven cases returned as enteric in the Native Army in 1897, in only three of the fatal cases was a *post-mortem* examination obtained, and in these three cases the lesion found 'support at least do not contradict the diagnosis made'. In all cases it was found impossible to trace the source of the infection.

The question of *post-mortem* examinations is most important. In private practice among natives of India and in the Native Army, it is quite the exception to get an autopsy, so that the diagnosis usually remains unverified; moreover it is probable that the death-rate from enteric among natives is not high; therefore, the vast majority of cases recover. We must, therefore, turn to jail statistics, for cases in prison are very unlikely to be overlooked, and moreover almost every prisoner who dies in jail is subjected to *post-mortem* examination, hence the peculiar value of jail statistics in this connection. On turning to the Sanitary Commissioners' Report, we find in 1896 in all the jails of India, twenty-one cases returned as enteric with seven deaths, and in 1897 thirty-four cases with fifteen deaths. The most of these cases were in all probability genuine enteric, or at least were cases clinically resembling enteric, and with ulceration of Peyer's patches found *post-mortem*. When we consider these few dozen cases among the many thousand cases of fever admitted to all the jail hospitals in India, it at once emphasizes the great rarity of the disease in adult natives. Moreover, when it is remembered, as the Sanitary Commissioner has frequently pointed out, that while the decennial ratio for the death-rate from enteric fever of European troops is 19 *per mille*, among Native Troops it is only 0.2, and among prisoners only 0.3 it shows the same fact. Again, the death-rate of European troops in 1897 from enteric fever was five times as great as that of the Native Army for all kinds of fever; therefore, whatever may be the nature of the remittent and continued fevers from which native soldiers suffer, it is clear that native soldiers and convicts are very much less liable to enteric than are European soldiers. We have often heard of enteric fever among Goorkhas, and

it is probable that it is more common among them than among other natives. On the other hand Captain C. Duer, F.R.C.S., I.M.S., the Junior Civil Surgeon of Rangoon, tells us he has never seen a case of enteric in a Burman. In this connection, we may remember, that tuberculosis is certainly common among both Goorkhas and Burmans, and we have long held that a long-continued fever in a Burman prisoner means tuberculosis, and we have never seen a case of enteric in a Burman prisoner. In fact, if we may be allowed here to relate a personal experience, the present writer, though in charge of large central jails for over seven years, has never yet seen a case of enteric fever, and he has never missed a *post-mortem* examination. On the other hand, in 1897, two jails, that of Nagpur and that of Mangalore, report cases. Major Andrew Buchanan's paper states the case very clearly for his large jail in Nagpur; but as regards the Mangalore cases, it will be enough to state that the Sanitary Commissioner considered the report 'imperfect'.

The result then of this brief review of the evidence before us points to the fact of the undoubted existence, as well as the undoubted rarity of the disease among natives of India. The figures for past ten years show an almost equal ratio of cases among sepoys and prisoners and they die much less from 'fevers' than the European soldiers; therefore it is clear that the question cannot be merely one of diagnosis. The fact seems to be that nearly every medical man in India can point to a few cases which he either proved to be enteric or which clinically strongly resembled enteric; but what are these few cases among the thousands of fever cases seen by every medical man during the year. In the General Hospital, Madras, we learn from figures kindly supplied by Drs. Brown and Maitland, in the year 1898, that there were 29 cases among Europeans and only five among natives, all the latter, it may be noted, being in young individuals. We are also much indebted to Lieut.-Colonel S. H. Browne, I.M.S., Principal of the Lahore Medical School, for an expression of his views on this matter. He informs us that during the past six years there have been only eleven native patients admitted into the Mayo Hospital for enteric fever; of these four died in hospital, and in two of them the diagnosis was confirmed at the autopsy. Three of the eleven cases were in children of 7, 11, and 11 years. The conclusions which Lieut.-Colonel Browne draws from his experience of the disease in the Punjab is that enteric fever is uncommon amongst natives; only 11 cases so diagnosed out of over 1,200 patients admitted for fever and carefully diagnosed in the wards proves this to be a fact. On the other hand, Colonel Browne has no doubt of the occurrence (though rarely) of this disease in natives. He says that one of the most beautiful and characteristic specimens of typhoid lesions

which he ever saw came from one of the Lahore cases above referred to. Another interesting note is added by Colonel Browne, *viz.*, that the prevalence of the disease has some connection with the dietary of the patients. Of the Lahore cases, two were in Native Christians, one in a man employed in a railway refreshment room, and one in a native of semi-European habits, a schoolmaster, and another in a cook from Srinagar. All these patients were meat eaters, and none of them strictly bound by caste rules. 'Nevertheless', adds Colonel Browne, 'I have known the disease to occur in a Brahmin'. He therefore inclines to the theory that the prevalence of enteric fever is connected with the dietary (apart from specific contamination of course) and that, as the native of India assimilates his diet to that of Europeans the more liable does he become to the disease.

It has been clearly shown above, and it is within the experience of all medical men in India, that while enteric fever is by no means unknown among Indians, yet it is undoubtedly comparatively rare among them.

When we leave the region of facts and come to try to consider the explanation of this lesser prevalence, we come upon less sure ground, and enter the region of conjecture. The theory which appears to us to have the greatest semblance to probability is that which points to a great protective evolution on the part of natives of tropical climates to this disease due to their former greater elimination by this disease. We must admit that enteric and imperfect sanitation go hand in hand. We must admit that in ancient days sanitation in India was practically *nil*; therefore, if these premises are correct, there must have been a very considerable elimination by means of enteric fever of the less resistant and a survival of the more resistant who would be able to leave offspring, who would inherit their peculiarities and be able to survive and continue the race in spite of the presence of the disease. If we believe in evolution, just as the presence of carnivora to any country must have called forth in weaker creatures (hares or antelopes) increasing powers of evading attack, so also the presence of any fatal disease during generations must tend to call forth, in the race attacked, a gradually increasing power of resistance to it. In fact enteric is now much less prevalent and fatal in natives as compared with Europeans just to the same extent, and for the same reasons as rinderpest is less fatal and less prevalent in India than in South Africa, where it has been recently introduced.

We must, however, leave this region of speculation, but recommend any of our readers who wish to follow out this line of thought to read the chapters on Physical Evolution in Dr. Archdall Reid's admirable volume published a few years ago entitled 'The Present Evolution of Man', in which it is shown that at

present man's evolution is not towards physical or intellectual strength as in his remote ancestry, but is mainly an evolution against disease and in town and city-dwellers mainly an evolution against diseases produced by living micro-organisms.

Current Topics, Etc.

Low Sodium Chloride Diets in Hypertension

(Reproduced from Medical Newsletter No. Wa 190, dated October 1949, issued by the American Medical Association)

THE authors present a study which was made in an attempt to evaluate the effects of restriction of dietary sodium chloride on the blood pressure of hypertensive patients. The group consisted of 22 patients who were placed on diets low in sodium chloride in the hospital. The effects of hospitalization and psychotherapeutic influences were controlled so far as possible.

In 13 patients, most of whom exhibited the disease in its severer stages, the response to salt restriction was poor. Three additional patients with milder forms of the disease manifested a lower level of diastolic pressure; in 1 of these the change which occurred was not reversed by the addition of salt to the diet.

A group of six female patients are described who exhibited obesity of a characteristic distribution, and some but not all of the signs of Cushing's syndrome. In these, levels of blood pressure appeared to be directly related to the intake of sodium chloride, being lower when salt was restricted and higher when it was added. These patients probably suffer from a disturbance of which arterial hypertension is only one manifestation.

It is suggested that there is an alteration of some of the functions of the adrenal cortex in such persons. In general, when the disease was relatively advanced and treatment was mandatory neither restriction of salt nor the rice diet appeared to be of much benefit.

(Schroeder, Henry A., St. Louis, Mo., *et al.*: Low Sodium Chloride Diets in Hypertension. *Journal of American Medical Association*, 140, 458-463, June 1949.)

Massive Penicillin Therapy of Abdominal Actinomycosis

(Reproduced from Surgical Newsletter No. Wa 193, dated October 1949, issued by the American Medical Association)

STANFORD AND BARNES point out that in the past abdominal actinomycosis has been a highly fatal disease. Although it comprises only 18 to 22 per cent of human actinomycosis, it is responsible for nearly 50 per cent of the fatalities from the disease. However, with the advent of sulfonamides and penicillin and their use in conjunction with adequate surgery and supportive therapy, there has been some improvement in the prognosis of this disease.

The course of events in two cases of severe abdominal actinomycosis indicates that infections of this type may not respond to penicillin therapy in rather large doses (800,000 units a day), sulfonamides, adequate surgery, and supportive therapy. These two patients

received this therapy over prolonged periods (eight and nine months). There was improvement for a time, and then progression of the disease.

It was then that really massive penicillin therapy was instituted. The first case history indicates that in the course of 67 days the patient was given 644,480,000 units of penicillin and 156 gm. of sulfadiazine. The second patient was given in the course of 48 days 586,400,000 units of penicillin; 500,000 units of penicillin were given intramuscularly every three hours and 10,000,000 units in 1,000 cc. of normal saline solution were administered daily by slow intravenous drip. Sulfadiazine was continued in doses of 6 gm. a day.

The only change in the treatment of these patients was the administration of massive doses of penicillin. Consequently, one may state with certainty that massive penicillin therapy has been responsible for the cures.

The apparent cure of an actinomycotic subphrenic abscess is noteworthy when the high mortality reported for these cases is considered. There have been 11 reported cases with only one patient alive after one year, and he had recurrence of the disease.

This report confirms the observations of others that massive doses of penicillin are not toxic even when given for relatively long periods.

Follow-up studies have shown cures of these two cases of one year's duration. The perfect health of the patients at this time leads us to regard these patients as permanently cured.

(Stanford, G. E., and Barnes, R. O.: *Surgery*, 25, 711-723, May 1949. The authors are connected with the Surgical Service, Veterans Administration Medical Teaching Group, Kennedy Hospital, Memphis, Tenn.)

Allergic and Vasomotor Rhinitis Treatment with Anthisan (Neoantergan)

By L. KNOX

(Abstracted from the *South African Medical Journal*, Vol. 23, 26th February, 1949, p. 155)

THIRTY-SIX cases of nasal allergy were treated with anthisan; 70 per cent, by adjustment of dosage, were given complete subjective relief so long as they continued to take the original minimal effective controlling dose. This figure is in accord with the results published by Feinberg *et al.* using benadryl and neoantergan, and by Calder using anthisan.

There is no evidence that when the drug has been taken for a long time, the effective dose gradually becomes smaller, nor is there any evidence of increasing tolerance.

There has been nothing in this series of cases to suggest that the long-continued exhibition of the drug over months produces any ill effects.

Atabrine against Tænia

(From the *Acta Medica Orientalia*, Vol. 7, November-December 1948, p. 223)

DURING prophylactic campaigns against malaria in South America it became known that atabrine exerts a specific effect against tænia and bothriocephalus. P. Barrelet (*Presse medicale* 73, 1948) tried this treatment in some cases of tænia saginata and bothriocephalus with excellent results. The procedure is as follows: The day before treatment the patient takes only milk. On the evening he has to make an extensive colonic



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lavage and in case of obstinate constipation the lavage is repeated the following day before the drug is administered. The next morning the patient receives 80 gr. of atabrine and has to stay in bed. After 4 hours he takes 30 gr. of sodium sulphate in 200 c.cm. water. If after two hours there are no bowel movements this dose is repeated. The treatment is well tolerated and no side effects have been observed.

Use of Estrogens in the Treatment of the Menopausal Syndrome

By H. H. BRAINARD

(Abstracted from the *American Practitioner*, Vol. 2, October 1947, p. 82)

THE widespread use of the estrogenic and estrogenic-like substances has led to their indiscriminate use in many instances. Their limitations, injudicious use and potential dangers should be emphasized.

The estrogens have their greatest use in the treatment of the menopausal syndrome. It has been estimated that only about 10 per cent of patients having symptoms during the menopause require treatment with the estrogens. It is customary at the present time to use this drug almost routinely for any one during this period. The effectiveness of the estrogens for the treatment of the menopausal syndrome is difficult to evaluate. Psychotherapy, placebos and sedation are as effective in the greater number of cases. The estrogens have been used for a wide variety of conditions other than the vasomotor instability during the menopause. Conflicting results have been reported for the treatment of leukoplakia, puritus vulvæ, arthritic pains, hypertension, cedema, intestinal pains, hyperglycemia, respiratory and circulatory disturbance, dysuria and incontinence and involuntional melancholia. When one considers the cessation of menstruation and the transition of the individual from the child-bearing period to one in which nature withdraws this function to protect her from the strain of pregnancy and childbirth, one can realize that this is an integral part of the process of aging and in no sense should it be regarded as a disease. Ovarian involution and the consequent estrogen withdrawal is only one of the many changes incident to the ageing process and it is difficult to believe how mere replacement therapy can greatly alter or control this complex symptomatology.

It has been previously stated that only about 10 per cent of patients undergoing the menopause should be treated with the estrogens. Their effectiveness is limited and the potential dangers from the prolonged administration do not justify their use except in the cases uncontrolled by psychotherapy and sedation. The first step in the treatment of the menopausal syndrome is to assure the patient that she is going through a normal process, that she does not have cancer that the excessive and injudicious use of 'shots' or 'injections' will only prolong the termination of her unpleasant symptoms and that with the cessation of menstruation she may be relieved of many of the distressing symptoms associated with the menses: fear of becoming pregnant, menstrual cramps and the general unpleasantness of menstruation. This form of psychotherapy along with mild sedation is sufficient in most cases. However, in a few cases, because of the severity of the symptoms, the estrogens are indicated. These should be given in such a manner that they can be terminated within a few months. Oral therapy should be tried first, giving stilbestrol 0.25 to 1 mg. daily at bedtime for a period of 20 days, followed by a rest of seven days. The dose should be kept at a minimum, explaining the reason so that at the end of several months the medication can be discontinued. Estrone sulphate may be administered in a similar manner if toxic symptoms arise from the use of stilbestrol. During this period an important supplement to this

treatment is the improvement of the general physical condition through vitamin therapy, the correction of any anemia, hypothyroidism, or other abnormalities that may exist.

The parenteral administration will be required in a relatively few cases. It should be administered in doses of 10,000 to 20,000 I.U. every four days for three to six doses, gradually increasing the interval so that the medication can be discontinued within six months. Many cases have had the medication continued for years with no programme of withdrawal, or no explanation given to the patient for discontinuing the therapy.

CONTRA-INDICATIONS TO ESTROGENIC THERAPY

Estrogenic therapy should never be used in the presence of carcinoma or following the treatment of any malignant disease. With irregular and increased bleeding which is so frequent during this period the estrogens should not be used; many instances have been reported where the bleeding stimulated by the estrogens has masked the development of cancer. A diagnostic curettage is always indicated if the bleeding does not cease after the estrogenic substance has been discontinued. However, many curettements are done needlessly because of the stimulation produced by the estrogens. The medication should never be used continuously, but rest periods should be interspersed every three or four weeks. Estrogens should not be given after radiation or x-ray has been used to control bleeding. I believe that the continued use of the estrogens over a long period of time produces severe mental trauma by prolonging the termination of the menopausal syndrome and keeping the patient in a continued state of mental unrest.

Carcinoma of the Rectum and Anus

By P. C. GUZZETTA

and
W. H. COLE

(Abstracted from the *American Practitioner*, Vol. 2, October 1947, p. 71)

Rectum.—Though the diagnosis of rectal carcinoma can be made readily by very simple means, it is still missed with unjustified frequency by many physicians, with dire consequences for the patient. The presence of rectal bleeding, change in bowel habit, or rectal pain should suggest a neoplasm and demand a rectal examination by palpation and proctoscope to rule out the disease. Approximately three-fourths of all malignancies in this area are palpable, and all of them are easily visualized with the proctoscope. It is obvious that at the present time the greatest advance in this problem can be made by earlier diagnosis of the lesion, and, preferably, by discovery of rectal polyps and adenomata which can be removed before they undergo malignant degeneration. It follows that to accomplish this, proctoscopic examination must be considered routine for all patients with rectal or anal complaints, and hæmorrhoidectomy should not be performed without previous examinations of this type.

Bleeding in rectal carcinoma is the most constant symptom and manifests itself usually as bright red blood either streaking the stool or in larger amounts, mixed with the stool. Massive hæmorrhage is uncommon; therefore anemia is usually a late manifestation. Change in the bowel habit may appear as constipation, diarrhoea, or alternating constipation and diarrhoea, and should be a signal for thorough gastro-intestinal investigation. Pain, which most frequently appears as a sense of rectal fullness, is quite variable and usually a late sign, due to the absence of sensory fibres in the rectum itself. It frequently signifies the invasion of surrounding more sensitive tissue, by the tumour.

Involvement of adjacent organs by direct extension and infection about the primary growth frequently

produces symptoms referable to the particular organ involved. The fact that hæmorrhoids and anal fistulæ are sometimes secondary to rectal carcinoma must constantly be kept in mind.

The appearance of a malignant rectal lesion on proctoscopic examination is so characteristic, with its indurated rolled edges and ulcerated central portion, apparently arising from normal mucosa, that the diagnosis is apparent even to the inexperienced. Biopsy is advisable for confirmation and as a basis upon which to judge the prognosis in the particular case. A negative biopsy calls for a repetition of the procedure.

There is no place for x-ray examination in the diagnosis of carcinoma of the rectum. In fact, it is inadvisable to force barium beyond the lesion for it will frequently complicate the subsequent operative procedure and it may mask the diagnosis. For this reason, it should be a standing rule that a barium enema will not be done in any case until a proctoscopic examination has been completed.

Anus.—The diagnosis of carcinoma of the anus rarely presents difficulty because of the relatively superficial location of the lesion. The presence of sensory nerve elements in the anal canal makes pain a prominent feature of this disease and usually brings the patient to medical attention at a comparatively early date. Biopsy will verify the diagnosis.

Clinical Trials of CAM-AQI in Malaria

By R. N. CHAUDHURI

and

N. K. CHAKRAVARTY

(Abstracted from the *Indian Journal of Malariology*, Vol. 2, September 1948, p. 115)

THE results of treatment of 55 cases of malaria with CAM-AQI have been presented.

Two regimes of treatment were tried: regime A, 0.1 gm. twice daily for 3 days and regime B, a single dose of 0.5 gm. These doses did not produce any untoward effect in any patient.

Fever subsided in an average period of 30 hours with regime A and 22 hours with regime B. Asexual parasites were not seen beyond an average period of about 24 hours with either regime. No other antimalarial drug interrupts an acute attack so quickly except chloroquine used in a much higher dose.

The drug had little or no action on the gametocytes. The *vivax* and *malariae* gametocytes disappeared within 5 days after treatment while crescents were seen up to 26 days.

Out of the 26 cases kept under observation for 1 to 8 months, there were 8 parasitic relapses and 1 clinical relapse. Relapse was more frequent with regime A than with regime B. Reinfection however could not be definitely excluded in all cases.

The drug appears to be equally effective in *vivax*, *falciparum* and *malariae* infections.

In view of the satisfactory response with a single dose CAM-AQI may prove a suitable remedy for mass treatment of malaria in rural areas.

Vitamin B₁₂

(From the *Medical Journal of Australia*, Vol. I, 12th February, 1949, p. 217)

VITAMIN B₁₂ is a crystalline substance recently isolated from liver extracts and found to produce hæmatological remissions in pernicious anæmia. It has been

available only in small amounts in the United States of America and its clinical use is still in the investigation stage, but preliminary reports suggest that it is a potent and important substance. An account of its use by four Harvard investigators, L. Berk, D. Denny-Brown, M. Finland and W. B. Castle, is of great interest, particularly because of the associated use of folic acid. The patient, a mulatto woman in her early forties, had been treated at the Boston City Hospital for some six years for pernicious anæmia. She had developed an allergic sensitivity in turn to pork-liver and beef-liver extracts, so that in 1946 treatment was commenced with folic acid, typical clinical and hæmatological responses occurring. Up to that stage no neurological changes had been demonstrable. The administration, at first intramuscular and then oral, of folic acid was continued rather irregularly till her readmission to hospital in May 1946. She then had a severe degree of anæmia and symptoms and signs of acute combined disease of the spinal cord. Folic acid therapy was discontinued, a diet free of fish, meat and eggs was prescribed, and no anti-anæmic treatment was given for four days. The neurological lesion continued to progress. A test of sensitivity to pork-liver extract produced a severe local and a serious systemic reaction. On the fifth day in hospital treatment was commenced with injections of vitamin B₁₂, after tests had demonstrated the absence of sensitivity to the substance (an important finding in itself). There was an almost immediate favourable response in both the hæmatological and the neurological conditions, that in the latter being especially remarkable. The therapy was discontinued for seven days from the ninth day of treatment, because of supply difficulties; her neurological condition began to deteriorate on the thirteenth day, but again began to improve five days after treatment was reinstituted. Progress from then on was steady and satisfactory in every way. Thus this crystalline liver derivative appears to be able to affect favourably both the hæmatological and the neurological conditions, associated with pernicious anæmia, though, as the report points out, there is nothing to indicate that it is more effective than liver extract. The question is discussed whether the neurological condition (which was evidently associated with a lesion as yet in great part reversible) may not have been due to the folic acid therapy, as the reports of other investigators have suggested; the improvement may then have been the result of cessation of this therapy. Against such an explanation it is argued is the progression of the neurological lesion during the first four days that the patient was under observation and the rapid and extensive improvement following the institution of vitamin B₁₂ therapy on the fifth day; especially significant is the slight setback during the interruption of the vitamin B₁₂ therapy with further recovery after its resumption. It seems that another major advance has been made in the analysis of the action of liver extract.

Nitrogen Mustard Therapy

(From the *Medical Journal of Australia*, Vol. 1, 4th June, 1949, p. 751)

RECENT medical literature has contained many references to the use of one or other of the nitrogen mustards in the treatment of the Hodgkin lymphosarcoma group of neoplastic diseases. This is one of the very few advantages accruing from the study of the action of substances devised for chemical warfare. The other outstanding dividend from this scientific advance in allegedly civilized communities is the introduction of BAL for arsenical and certain other metallic poisonings. We should, however, be thankful for the beneficent effect of the nitrogen mustards, since they have stimulated thought on a very controversial subject. It has in the past been gratifying to see how

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References : Shortage of space precludes list of references but full documentation may be obtained on application to :

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rapidly radiosensitive tumour masses shrink and disappear under correctly applied irradiation but depressing to witness the inevitable recurrences. Of course, we are here opposed to a biological principle; for it seems as if the Mr. Hyde among bacteria, viruses or metaplastic cells is nearly always present and potent and ready to rally his assaults against the weaker Dr. Jekyll presiding over the destinies of the body's mutable protoplasm. Varying the metaphor, there are left a few cells which, 'stout as Julius Caesar', are proof against the wave-lengths of the radiotherapist's piper. It is in the renewed attack on these that the nitrogen mustards have been temporarily successful, the response being sometimes dramatic. Review of the literature shows now an imposing number of encouraging results, even if they are not lasting. A couple of these may be quoted. Andrew H. Meyer and W. C. Overmiller report two cases of Hodgkin's disease and three of lymphosarcoma treated with the methyl bis (β -chloroethyl) amine hydrochloride. The former patients remain well after eight to ten months; two others who died were relieved substantially for a time. The toxic effects known to be not infrequent accompaniments of the drug occurred more or less in all these patients, but were not a source of anxiety. These are, as is now well known, connected chiefly with the bone marrow, whose blood cell forming functions are deranged and depressed by the drug, chiefly within the first three weeks after administration. Local effects are not serious if care is taken to prevent escape of the solution from the vein used for the injection, and symptoms such as vomiting and diarrhoea are only transitory.

S. Ben-Asher reports a series of some size, part of which is being collected for the National Research Council of the United States of America. Twenty-nine patients were studied, suffering chiefly from Hodgkin's disease, but also from lymphosarcoma and different varieties of leukaemia. Most of the patients with Hodgkin's disease were in the advanced stages, and had had previous x-ray treatment, but most of them had remissions from one or more courses of nitrogen mustard. In a few cases in which the condition had been shown to be resistant to irradiation the results were striking. In lymphosarcoma and the different types of leukaemia the results were not so good, and remission was often soon followed by relapse and death. A series of patients with carcinoma of the lung were also included, but it is hardly surprising that with them no good results were obtained. Toxic effects of the drug on bone marrow function were observed, but were not severe. Toxic nausea and vomiting were commonly seen, but sedation before treatment lessened this complication. It seems from results such as these that some differentiation may now be made between the types of lymphoid neoplasms which may be expected to respond to nitrogen mustard and those which may not. This brings us back to one of the highly controversial subjects in connection with this group of diseases, their classification. There is clear evidence of recent years that medicine has suffered from being too highly descriptive. It is freely admitted that a true aetiological classification is not possible, at least not when widely applied to the whole clinical field, but there has been too much deference to the so-called 'classical' pictures, whether these relate to a clinical syndrome or to the histological or biochemical findings in body tissues or fluids. Even so simple an example as the mutability of epidemic disease illustrates this.

R. P. Custer and W. G. Bernhard in a recent article plead for a more comprehensive view of the Hodgkin lymphosarcoma group. They point out that as far back as 1907 Coley suggested that lymphosarcomatosis would be a better name for Hodgkin's disease, and that the many histological arguments that have been brought up since have laid emphasis on the need to recognize the reticulum cell as the parent from which a number of neoplastic variants spring. Cases may be found in the literature of reticulum cell sarcoma with

a clinical picture of either lymphatic or monocytic leukaemia, and, though it may seem at first somewhat remote, *mycosis fungoides* has also been brought within the same classification by some authorities. Leukaemia in particular is overdue for some revision of definition and outlook; it is still usually described as a condition in which an increase of the peripheral white blood cells is present. Custer and Bernhard state that the descriptive terms generally employed in this wide group of disorders should 'designate the predominating histologic pattern of a lymphoma at the time of a particular examination of tissues or blood'. In a series studied by them they found that the histological pattern underwent virtually complete alteration in 39 per cent of 135 cases in which biopsy was carried out and autopsy was performed later. Although it is more difficult to think in terms of pathological changes, especially when these vary, truth in diagnosis and hope in therapy are more likely to be attained if this is done. It needs more mental effort than does the use of well-worn pigeon-holes, and may perhaps increase possible attrition with patients' friends and with an inquisitive lay Press seeking 'tabloid' information, but it should be worth while.

The Use of Quinidine in Hiccup

(From the *Medical Journal of Australia*, Vol. 1, 4th June, 1949, p. 750)

Hiccup has been the subject of comment from time to time in literature ranging from fiction to medical journals. It may be merely a social embarrassment, a time-worn cause for jesting, or an ominous clinical sign. The number of different causes of this uncomfortable phenomenon is legion, for it may arise from disturbances affecting the central or peripheral nervous system, or the organs in the chest or the abdomen, from infections, or from the presence of toxic products in the body fluids. The number of forms of treatment is correspondingly large and these range from domestic manoeuvres, some of them grotesque, to surgical procedures. Samuel Bellet and Carl S. Nadler, in treating patients in the cardiac wards of a large general hospital, noticed that the exhibition of quinidine to patients with severe hiccup occurring in relation to cardiac and renal insufficiency caused the cessation of the hiccup. At least hiccup which would not respond to such measures as sedatives, antispasmodics, oxygen and carbon dioxide, disappeared each time the drug was given. The first patient was given fifty grains of quinidine in a period of nine days and relief followed within two hours of each administration. Cardiac irregularity due to extrasystoles was also controlled. The next patient, who had advanced caecous tuberculosis of the lungs and prerenal azotemia, was relieved by a single intramuscular dose of nine grains of quinidine, followed by maintenance doses given by mouth. In another case the intravenous route was chosen, as it was found that parenteral administration was more satisfactory than the oral method. The initial success with a patient, who was in any case a good subject for the use of quinidine, led the authors to try the effect of the drug in a variety of conditions, the only common factor being the existence of invertebrate hiccup. Nine patients were so treated; only in one instance did the method fail entirely; in two the result was very satisfactory. In discussing the probable mechanism, Bellet and Nadler point out that they expected from high dosage over a short period of time so as to ensure high concentration in the body. Their experience being so limited, they can suggest only the optimum dosage, but place this tentatively at ten grains given intramuscularly, repeated every hour for two or three doses. A low maintenance dose

may be given thereafter if needed. They do not advise that the drug be used for all patients, but think it is worth trying for all patients who persist with hiccup in spite of the trial of all other ordinary methods. The mechanism of action is probably bound up with the effect of quinidine on striated muscle in lengthening its refractory period. The pharmacology of quinine and related substances is briefly reviewed in this article; two familiar clinical points may be recalled here, the value of quinine in *myotonia congenita*, and also in the relief of night cramps of the extremities. In a brief after-note the authors justly remark that where hiccup is associated with abdominal conditions which have necessitated operation, it is most important to relieve any imbalance in the electrolytes, as this may be an important factor. This may surely be taken for granted in the light of modern post-operative treatment for abdominal lesions. But it seems as if some further trial of quinidine and its relations may be worth while in an attempt to relieve a condition which can be extremely distressing, especially to a patient severely ill.

Marrow Biopsy

(Abstracted from the *Lancet*, i, 26th March, 1949, p. 530)

THE hazards of sternal puncture, to which we referred last year, have been investigated by Rubinstein, who concludes that fatalities are much commoner than the literature might suggest. He therefore advocates the alternative method of aspirating bone marrow from the iliac crest.

This is generally a less painful operation; and it can be carried out with safety on small children. Rubinstein claims further advantages for this method, which he has practised more than a thousand times. To the operator it is a relief to know that, with the needle directed downwards from the iliac crest towards the lower extremity, there is no danger of penetrating an inner plate; moreover, for serial examinations the two crests offer a choice of site. Rubinstein made parallel studies on sternal and iliac marrow in 216 patients. In those with normal findings (their ages ranged from 16 to 78) the iliac crest always provided haematopoietically active marrow; and the cell distribution showed approximately the same range as sternal marrow. In general this parallelism existed also in pathological marrows, but iliac aspiration yielded fuller information than sternal marrow in four groups. Firstly, in 3 patients whose sternal marrow had repeatedly proved hypocellular, iliac puncture revealed the classical cytology of leukaemia which was later discovered also in the sternal marrow. Secondly, in 3 cases of multiple myeloma where sternal puncture was inconclusive, the diagnosis was indicated by iliac-marrow films; and in 2 of these with thrombocytopenia and a bleeding tendency, the material obtained by sternal puncture was too diluted with blood to be of real use. Thirdly, in some instances of aplastic anaemia and osteosclerotic anaemia sternal puncture revealed an aplastic bone marrow, while by iliac aspiration islands of active haemopoietic tissue were found; in other cases, however, the reverse held. Finally neoplastic cells were found more commonly in marrow from the ilium than from the sternum.

With research workers the ilium is already a favourite source of marrow, and the method described by Rubinstein will probably be increasingly popular with clinicians. A further method, by which marrow is aspirated from the spinous processes of the vertebrae was described in 1936 by Heidenreich and Heidenreich, and has been used with success by de Weerd. In 25 patients, all in hospital with upper-respiratory infections, samples of marrow from spinous processes

and from the sternum were found to be remarkably similar; and it is noteworthy that in 2 elderly patients, aged 75 and 72, the cellularity of the vertebral marrow was equal to that from the sternum. When questioned 13 of the patients said that they preferred the vertebral approach and 7 the sternal method; 5 expressed no preference. Loge, though not suggesting that the sternal technique should be discarded, points to the value of an alternative approach, especially in young children, where the risks of sternal puncture are greater than in adults.

One method of marrow biopsy may succeed where others fail; and haematologists are likely to make increasing use of the alternatives to sternal puncture.

Air Embolism during Transfusion

(From the *Lancet*, i, 30th April, 1949, p. 743)

DURING the war, the need to restore blood volume rapidly in cases of severe oligæmic shock led clinicians to assist the inflow of blood or plasma by raising the air-pressure in the transfusion bottle, for which purpose they used a Higginson's syringe attached to the air inlet tube. The practice thus introduced has been continued; but it is definitely dangerous unless the transfusion is closely and constantly watched while the air-pressure is being raised. In our present issue Dr. Doyle and Dr. Frodsham repeat the warning already given by Dolton *et al.* They draw attention once more to the possibility of air embolism when the bottom part of the filter within the bottle becomes blocked or partly blocked with blood-clot, and the air under pressure takes the path of less resistance through the top of the filter exposed above the blood and thus passes through the rubber tubing into the vein. In the case they record the glass outlet-tube of the bottle apparently projected some 2.3 cm. above the rubber bung; so, if this filter had not become blocked by clot, air would have been pumped into the vein while the level of the blood was still about an inch above the rubber bung.

The lesson to be learnt from these accidents is that raising the air-pressure within the transfusion bottle is legitimate only if undertaken with extreme care. Doyle and Frodsham's suggestion that it should only be performed by a doctor is a good one and might well be generally adopted. Similarly, the air-pressure should not be raised by using a Higginson's syringe when the level of the blood has fallen below the filter, since it is impossible to see whether the blood contains clots. Unfortunately it is difficult to ensure that blood is collected without formation of any clot. The acid-citrate-glucose anticoagulant of Loutit and Mollison, now in general use, contains twice as much citrate as is theoretically necessary to prevent coagulation; but clots may still form unless the blood and acid-citrate-glucose solution are shaken during collection, and it is important that particular attention should be paid to this detail of technique when donors are being bled.

Prevention of Sunburn

(From the *Lancet*, i, 30th April, 1949, p. 744)

IN Britain sunshine is seldom a burning problem; and this perhaps explains why most of the recent work on protecting the skin against the sun's rays seems to have been done in America. A year or two ago Luckiesh and Taylor suggested the application of a refined grade of petrolatum with 10 per cent salol in yellow petrolatum U.S.P. Since then Shaw has recommended topical application of a 5-10 per cent solution

of *p*-aminobenzoic acid in 70 per cent alcohol, while Sulzberger and Bayer have reported good results from applying the acid in 10 per cent alcoholic solution and in oil-in-water emulsion creams, esters of *p*-aminobenzoic acid have also proved satisfactory. When alcoholic solutions are applied, the alcohol evaporates leaving a film of powder, which is rubbed into the skin. Shaw claims that by this method patients who were extremely sensitive to sunburn were able to expose themselves for 8-12 hours to intense sunshine in Florida and Mexico, without the slightest discomfort, but he observed that, while *p*-aminobenzoic acid was often effective in protecting people suffering from lupus erythematosus, it was ineffective in photosensitization dermatitis.

A further substance now advocated as a preventive of sunburn is phenazone (antipyrin), which is said to be efficient in various vehicles and concentrations. This chemical has the merit of being readily available; but when given internally it can cause skin eruptions, and with repeated applications to the skin it may perhaps produce sensitivity.

Suprarenal Hormone in Rheumatoid Arthritis

(Abstracted from the *Lancet*, i, 7th May, 1949, p. 786)

LAST week we referred to the startling results achieved at the Mayo Clinic in the treatment of rheumatoid arthritis by a suprarenal hormone. Dr. Philip Hench, who is primarily responsible for this development, suggested in his Heberden oration last year that rheumatoid arthritis is potentially reversible; he showed that sometimes this disease apparently undergoes spontaneous cure and that the remissions associated with pregnancy and jaundice are far more satisfactory and commoner than those associated with any form of treatment, including chrysotherapy. These ideas he has reiterated this year.

The first report on the new treatment appears to substantiate Hench's suggestion. The adrenal extract used is Kendall's 'compound E', the formula of which is 17-hydroxy-11-dehydrocorticosterone. In each of 14 patients with moderate or severe rheumatoid arthritis, improvement began a few days after intramuscular injections of this compound were started; pain stiffness and limitation of movements were reduced, and tenderness and muscular pains relieved; appetite and weight improved, and 'toxicity' was replaced by a sense of well-being; and the blood-sedimentation rate fell. The work was controlled by substituting injections of cholesterol for compound E without the knowledge of the patients or the clinical observers; the result of each substitution was an exacerbation of the rheumatic process which was almost as striking as the effect of treatment.

As Hench points out, many further investigations must follow. Dosage, prolonged administration, and possible toxic effects must all be studied. In a chilling footnote Messrs. Merck and Co., its manufacturers, say that no supplies will be available before 1950—and very little even then.

Specific Therapy of Bacterial Infections of Central Nervous System

By H. F. DOWLING *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 139, 19th March, 1949, p. 755)

THERAPEUTIC agents are now available to combat most bacterial infections of the central nervous system. Consequently, proper treatment depends on (1) prompt

diagnosis of the disease, (2) prompt determination of the aetiological agent, and (3) selection of the appropriate drug of antibiotic.

Meningitis. This is the most frequent type of bacterial meningitis. Results have been obtained with penicillin, sulphonamides, and chloramphenicol. The dose of adults is 6 gm. immediately and 1 gm. every four hours and for children 70 mg. per kilogram (1 grain per pound) of body weight immediately and 150 mg. per kilogram (1 grain per pound) for each twenty-four hours thereafter, at four-hour intervals. Comatose patients should be given an initial intravenous dose of 0.5 per cent solution of the sodium salt in sixth-molar lactate or isotonic sodium chloride solution. Subsequent doses are preferably given by stomach tube or by mouth, since this insures more constant blood levels, although the subcutaneous route may be used instead. Sodium bicarbonate, 6 gm. at the start and 3 gm. every four hours, should be used concomitantly in order to minimize the possibility of the formation of renal calculi.

We have not found it necessary to employ penicillin routinely in meningococcal meningitis except in patients with a fulminating infection (the Waterhouse-Friderichsen syndrome). It is also used in patients who do not respond to sulphonamide drugs within twenty-four to forty-eight hours. Probably the most satisfactory way to administer penicillin for these purposes is in doses of 1,000,000 units intramuscularly every two hours.

Treatment with sulphonamide compounds and penicillin may be discontinued one week after the temperature drops if the patient is doing well in all other respects. The fatality rate for cases in our series was 8.8 per cent and increased progressively with age. The fatality rate for comatose patients was double that for the entire series.

Pneumococcal meningitis.—This is the most frequently observed disease in this group.

Previous studies in our laboratory have shown that several factors are important in obtaining and maintaining a satisfactory concentration of penicillin in the cerebrospinal fluid: (1) sufficiently large amounts of penicillin must be administered systemically; (2) the penicillin must be given for a certain interval before it appears in the cerebrospinal fluid, and (3) penicillin diffuses into the cerebrospinal fluid more freely in the presence of inflammation. We therefore advocate as the best treatment for pneumococcal meningitis available to-day 1,000,000 units of penicillin intramuscularly every two hours. Patients in coma or in extremis when treatment is begun may be given a single initial intrathecal dose of penicillin in addition. Sulphonamide compounds do not appear to be necessary when these doses are used.

Meningitis caused by staphylococci and beta streptococci.—Meningitis caused by these organisms is usually treated by multiple intrathecal injections plus systemic doses of penicillin. We have successfully treated one patient with meningitis caused by beta haemolytic streptococci with systemic doses of 1,000,000 units of penicillin every two hours and without intrathecal therapy.

Haemophilus influenzae meningitis.—This type of meningitis responds well to streptomycin. Infants and young children may be given 1.5 gm. per day, divided into 4 six-hour intramuscular doses. Adults should receive 5 gm. per day. Daily intrathecal injections of 25 mg. are also given to young children and 50 mg. to older children and adults.

Although streptomycin is usually successful when given alone, we believe that sulphadiazine should be given at the same time because of its effect on *H. influenzae*, because it may help to prevent the appearance of streptomycin-resistant organisms and because it will inhibit the multiplication of Gram-positive organisms during streptomycin therapy.

When treatment is delayed or the patient is critically ill when therapy is started, or if no improvement occurs

after forty-eight hours of streptomycin-sulphadiazine therapy, specific rabbit antiserum should be given in doses of 100 to 200 mg. of antibody nitrogen. About 90 per cent of patients will recover when they are treated in this manner.

Tuberculous meningitis.—The early results with streptomycin in this disease appeared to be excellent. Clinical arrest occurs in one-fourth of the patients. The results are especially favourable in patients who had meningitis without miliary tuberculosis. Not all of the patients with arrested disease recover, however. The longer they are followed the higher becomes the percentage of relapses, until now it seems likely that no more than 5 or 10 per cent of patients with tuberculous meningitis will recover completely and most of these will have some permanent neurologic damage. A ray of hope is offered by the results of Lincoln and her associates. They obtained clinical arrest in 6 of 7 patients treated with a combination of streptomycin and promizole (4, 2'-diamino-phenyl-5'-thiazolyl sulphone). Prolonged follow-up on these patients as well as further studies on combinations of streptomycin and various antituberculous chemicals will be welcome.

Patients with tuberculous meningitis should be treated as early in the course of the disease as possible with intramuscular doses of 9 mg. per kilogram of body weight per day, up to a maximum of 2 gm., at six-hour intervals. Intrathecal doses of 1 mg. per kilogram, up to a maximum of 50 mg., are also given, at first at daily intervals and after two weeks on alternate days. It is usually recommended that treatment be continued for four months, but it is doubtful whether streptomycin is of any value after six to eight weeks. The spinal fluid leukocyte count and protein content are no criteria of recovery. More reliable are the absence of organisms in smear and culture and a return of dextrose content to normal.

LOCALIZED INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

The same procedures should be used in the treatment of abscesses as are used in meningitis. The causative organism should be determined and the proper antibiotic or sulphonamide compound should be used. Surgical drainage with local instillation of the proper antibiotic should be employed where advisable.

Experiences with Nitrogen Mustard Therapy

By C. C. SHULLENBERGER *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 139, 19th March, 1949, p. 773)

UNTIL recently, the palliative treatment of lymphoblastoma and other neoplastic diseases has depended almost entirely on the use of irradiation by roentgen rays or radium. With the recent introduction of the nitrogen mustards as potential therapeutic agents in this field, a concentrated effort has been made by various groups of investigators to determine whether there are any specific indications for the use of these substances in place of, or as an adjunct to, irradiation therapy. Since it appears that the biologic effects of the nitrogen mustards and the qualitative clinical response caused by them are similar to, if not identical with, those exerted by irradiation, and since their availability and ease of administration confer definite advantages over irradiation therapy, it becomes a matter of some importance to know what may be expected to these agents when they are employed under certain clinical conditions.

METHOD OF TREATMENT

The nitrogen mustard employed in all of the cases which form the basis of this report was methyl-bis

(B-chloroethyl) amine hydrochloride. With few exceptions, a course of treatment consisted of intravenous injections, on four consecutive days, of 0.1 mg. of this material per kilogram of body weight. The total dose for any course, therefore, was 0.4 mg. per kilogram of body weight. In a few cases, it was necessary, because of excessive nausea and vomiting, to lengthen the interval between injections or to terminate the treatment after two or three injections, instead of the usual four, had been administered. It has been our experience that 150 to 200 mg. of pyridoxine hydrochloride, given intravenously at the time of the injection of the nitrogen mustard, often will reduce the severity of the nausea and vomiting which so frequently follow the administration of the latter. As a general rule, we have permitted six weeks to elapse between any two courses of nitrogen mustard; although, in a few instances in which more intensive treatment was indicated and the blood cell counts were satisfactory, we have given a second course between four and six weeks after the first.

SUMMARY AND CONCLUSIONS

This paper includes an analysis of the results of nitrogen mustard therapy, or combined nitrogen-mustard and irradiation therapy in 18 cases of advanced Hodgkin's disease. Our experience indicates that, in cases in which the disease has become more or less refractory to roentgen therapy, nitrogen mustard has very limited usefulness as an agent which may produce transient subjective improvement without necessarily altering or significantly delaying the progressive course of the disease. It is apparent that existing lesions may progress or that new lesions may develop within a few weeks to a few months after institution of nitrogen mustard therapy. Very satisfactory regression of some of the lesions in a given case may occur as a result of this therapy, while progression of other lesions is taking place simultaneously. Lesions which involved non-lymphoid organs responded poorly or not at all to this therapy. Our results suggest that the cases in which there was the least tendency to progression during the period of observation were those in which the disease had existed for the longest time prior to the institution of nitrogen mustard therapy.

The results of nitrogen mustard therapy in 10 cases of lymphosarcoma also have been considered. While the over-all results were not encouraging, in our experience they were unpredictable. While 7 of 10 patients either died within six months or were unimproved after this therapy, it appears that some patients may respond very well to it. From our experience, we cannot draw any conclusions as to the correlation between the histologic pattern in a given case of lymphosarcoma and the responsiveness to therapy.

In our hands, nitrogen mustard has been a valuable adjunct to roentgen rays in the treatment of mycosis fungoides, although its usefulness varies in different cases. A very satisfactory result was obtained with nitrogen mustard therapy in a case of cutaneous lymphoblastoma after irradiation had failed to stop progression of the disease. Initial results in the treatment of polycythemia vera with nitrogen mustard have been sufficiently encouraging to warrant further investigation of its usefulness in this disease. Malignant neoplasms have responded very poorly or not at all to nitrogen mustard therapy in our experience.

Nitrogen mustard is potentially a dangerous drug and is capable of severely damaging the hæmopoietic tissues when used in the presently accepted therapeutic doses. Finally, we believe that a true evaluation of the efficacy and reliability of nitrogen mustard in cases of lymphoblastoma can be determined only by employing this agent alone in a series of hitherto untreated patients and comparing the results with those obtained in treating similar patients with irradiation and with a combination of irradiation and nitrogen mustard.

